The social determinants of glycaemic control in type 2 diabetes mellitus

Stopford, Rosanna Elisabeth Alice

Awarding institution:
King's College London

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Rosanna Stopford

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University of London

Department of Psychological Medicine

Institute of Psychiatry

King's College

University of London

Abstract

The social determinants of health are important contributors to health inequalities and have prognostic significance for biomedical profiles, morbidity and mortality. Despite this, in type 2 diabetes, there is a focus on the traditional medical model of care with little emphasis on the social contexts within which individuals are embedded. The primary aim of this thesis was to identify the social determinants of glycaemic control over 2 years in individuals with newly diagnosed (< 6 months duration) type 2 diabetes.

A prospective cohort was used. Individuals with newly diagnosed type 2 diabetes were recruited from primary care centres in 3 adjacent boroughs of South East London. The setting was multi-ethnic and socio-economically diverse. Socio-demographic, biomedical, psychological and social data were collected using standardised data collection schedules, clinical assessments and from medical records. The main outcome was HbA1c (mmol/mol) at 2 years. Mixed effects multi-level models were used to investigate associations between social variables and HbA1c when accounting for relevant confounding and clustering within general practices.

From 96 general practices, 1447 participants were recruited between September 2008 and November 2011. Their mean age was 56 years (±11.06), 55% were male and 51%, 38% and 11% of the sample were white, black and south Asian/other ethnicities respectively. In multi-level models neither social support nor the neighbourhood environment were significantly associated with HbA1c at 2 years after correcting for multiple testing.

Type 2 diabetes is a major and growing burden to the individual and to society. Current models of social mechanisms for ill health do not appear to apply to people at the time they are diagnosed with type 2 diabetes, but this does not mean they are not

important. These findings may suggest that social processes in the natural history of type 2 diabetes are more complex than originally presumed. They highlight the need to revisit and potentially, re-define the conceptual underpinnings of social theories to be applicable to type 2 diabetes.

Acknowledgements

I am extremely fortunate to have been given the opportunity to complete my PhD at the Institute of Psychiatry, King's College London. I would like to take this opportunity to acknowledge those individuals who have made this thesis possible and in doing so, making it an unforgettable experience.

This thesis would not have been possible without the expert guidance and support of my supervisors, Professor Khalida Ismail and Dr Kirsty Winkley. I have been fortunate to be mentored by Professor Ismail throughout my MSc and my PhD. She is an inspiration on both a professional and personal level. Her high standards and rigorous approach to research have been critical to my learning and have provided an exemplary basis for my future endeavours. She has demanded effort and expected excellence - I will continue to strive towards emulating her professional standards. My deepest gratitude is also extended to Dr Winkley, who has been so generous with her time and expertise. Her calm approach has been invaluable and I remain enormously appreciative for all her encouragement and guidance.

I would like to thank Professor Stephanie Amiel. Despite not being my supervisor, Professor Amiel has offered expert feedback, guidance and a listening ear. It has been an honour to work in her team. My appreciation also goes to Dr Daniel Stahl for his time, and particularly his patience, when offering statistical advice

I will always be indebted to the National Institute for Health Research, the funding source that has made my PhD possible.

A special thank-you goes to the participants of the SOUL-D study who were so generous with their time and without whom, this thesis would not have been written.

I have been lucky to have made so many great friends throughout this project, and want to extend my thanks to all the people in the SOUL-D team, past and present, who have made the experience such a joy: Gemma Knight, Lindsey Marwood, Emma Britneff, Sarah Mann, Linda East, Jennifer Hunt, Helen Graves, Jean-Pierre Laake, Katherine Twist, Chris Garrett, Cynthia Mohandas and Nicole DeSoyza. Thank you for encouraging me in times of doubt, inspiring me when the final chapter seemed so far away, and most of all, for entertaining me throughout.

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daily 7am phone calls and boundless enthusiasm offered such encouragement and were gratefully received at times when my own enthusiasm was lacking. Thanks also go to Natalie, the most generous of landladies and the kindest of friends.

I dedicate this thesis to my family, present and absent.

Statement of Contribution

This thesis is embedded within the South London Diabetes (SOUL-D) Study, a National Institute for Health Research (NIHR) Programme Grant funded observational study. The Principal Investigator is Professor Stephanie Amiel and the Co-Principal Investigator is Professor Khalida Ismail. The NIHR programme grant manager / NIHR Post-doctoral Fellow is Dr Kirsty Winkley. The Principal Investigators designed SOUL-D. The primary aim is to investigate the association between depression and glycaemic control in individuals with newly diagnosed type 2 diabetes.

I first worked on the SOUL-D Study during my MSc (September 2009 – August 2010) where I competed my dissertation, then as a research assistant (September 2010 – December 2010) and subsequently as a PhD student on NIHR funding (January 2011 – March 2014).

My responsibilities and contributions to the SOUL-D study were as follows:

Recruitment and follow-up

I contributed to data collection, both at recruitment and follow-up stage, between September 2009 and September 2013. When I joined SOUL-D, 1013 participants had already been recruited and 348 had been followed-up at year 1. Over the past 4 years I recruited 76 (3%) participants at baseline and conducted 417 (17.5%) (Year 1: 231; year 2: 186) follow-up appointments. I also recruited 3 surgeries into the study.

Assessment of Attrition

I took responsibility for the assessment of attrition. If participants had moved out of the study area, I liaised with NHS organisations in order to re-establish contact with these individuals. Where this was possible, with permission, I sent data collection schedules by post to participants' home address, I also approached their new GP surgeries to obtain biomedical information. Where participants had died, I ordered death certificates.

Training and supervision

I was responsible for the training and supervision of new staff members and students. I supervised 2 MSc students during the course of my PhD who also contributed to SOUL-D data collection.

I also supported the Principal Investigators in the day-to-day running of SOUL-D, for example covering colleagues on leave, coordinating and collaborating with other researchers in workload management, data management and office management.

Presentations

I presented research at the Diabetes UK Professional Conference, the David Pyke and Peter Watkins Conference at King's College London and at departmental seminars. I have also represented the SOUL-D team at King's College Hospital open days. Alongside an MSc student, I organised and conducted a Patient and Public Involvement

Group at Guy's Hospital, where I presented the theoretical framework of my PhD and received valuable feedback. I have also designed SOUL-D newsletters which aim to update participants and GP surgeries on the progress of SOUL-D and any preliminary findings.

PhD Design

Although I was not involved in the original design of SOUL-D, I lead the formulation of my research question and all hypotheses tested in this thesis. The demographic, social support and biomedical variables were routinely collected as part of SOUL-D. The 6 neighbourhood variables included in this thesis (with the exception of one: perceived neighbourhood problems) were not routinely collected. I collected this data from external sources. I collected all raw data used in the Geographical Information Systems (GIS) analysis and prepared all data for analyses. Due to the complexity of the programme the analyses using GIS were run externally. The MSc students assisted with checking geocoded coordinates used in Chapter 8.

Dr Daniel Stahl (Department of Biostatistics, Institute of Psychiatry) supervised and gave advice on the power calculation in Chapter 5, on the assessment of normality, which is reported in the statistical plan in the methodologies, and on the multi-level analyses in Chapters 7 and 8. I performed all statistical analysis in this thesis.

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Glossary of Abbreviations

BMI: Body mass index

CABG: Coronary artery bypass graft

CI: Confidence interval

DCCT: The Diabetes Control and Complications Trial

DESMOND: Diabetes Education and Self Management for Ongoing and Newly Diagnosed

GP: General Practice

GIS: Geographical Information Systems

HbA1c: Glycated haemoglobin

HDL: High density lipoprotein cholesterol

IDF: International Diabetes Federation

IFCC: The International Federation of Clinical Chemistry

IMD: Index of Multiple Deprivation

IQR: Interquartile range

LDL: Low density lipoprotein cholesterol

MI: Myocardial infarction

NHS: National Health Service

NICE: The National Institute for Health and Care Excellence

NIHR: National Institute for Health Research

NS-SEC: National Statistics Socio-Economic Classification

RCT: Randomised controlled trial

SD: Standard deviation

UK: United Kingdom

UKPDS: United Kingdom Prospective Diabetes Study

US: United States

WHO: World Health Organisation

Chapter 1 Diabetes mellitus

1.1 **Synopsis**

This chapter will set the context of this thesis which is a study of the social determinants of glycaemic control in individuals with newly diagnosed type 2 diabetes. In this chapter I will consider the current epidemic of type 2 diabetes, its epidemiology, management and associated complications with a particular emphasis on the social dimension of the disease. I will introduce the concept of the social determinants of health and propose an epidemiological model of the social determinants of glycaemic control in type 2 diabetes.

1.2 **Introduction**

Diabetes is a major public health concern and an increasing challenge to healthcare systems globally. The worldwide increase has reached pandemic proportions and is rising in parallel with the obesity epidemic. Diabetes, if diagnosed late, left untreated or poorly managed can lead to life threatening complications and premature death. In the United Kingdom (UK) alone, there are an estimated 20,000 avoidable deaths each year as a result of the sub-optimal management of diabetes. In addition to immense human suffering, diabetes accounts for disproportionate healthcare expenditure, loss of productivity and decreased rates of economic growth. The increasing costs and pressure placed on healthcare systems globally are not sustainable. To date, the prevention and management of diabetes has focused on the conventional medical model but improvements cannot be solved by healthcare systems alone. Whilst, undoubtedly, biological interventions can improve prognosis and prevent some adverse outcomes it may be just as important to consider the conditions that cause ill health in the first place. Broadly, these can be conceptualised as the conditions into which we are born, grow, live, work, and age and are referred to as the social determinants of health. Such an approach is a necessary step towards advancing the understanding of diabetes in the modern age and the contexts within which medical or behavioural interventions may succeed.

1.3 **The prevalence of diabetes**

Diabetes is a global health problem. Epidemiological evidence indicates that without strategies to prevent and control diabetes, the prevalence will continue to increase. The International Diabetes Federation (IDF) estimates that 371 million people have diabetes, half of whom are undiagnosed. This figure is set to increase to 438 million by 2030 (IDF 2012) (Figure 1).

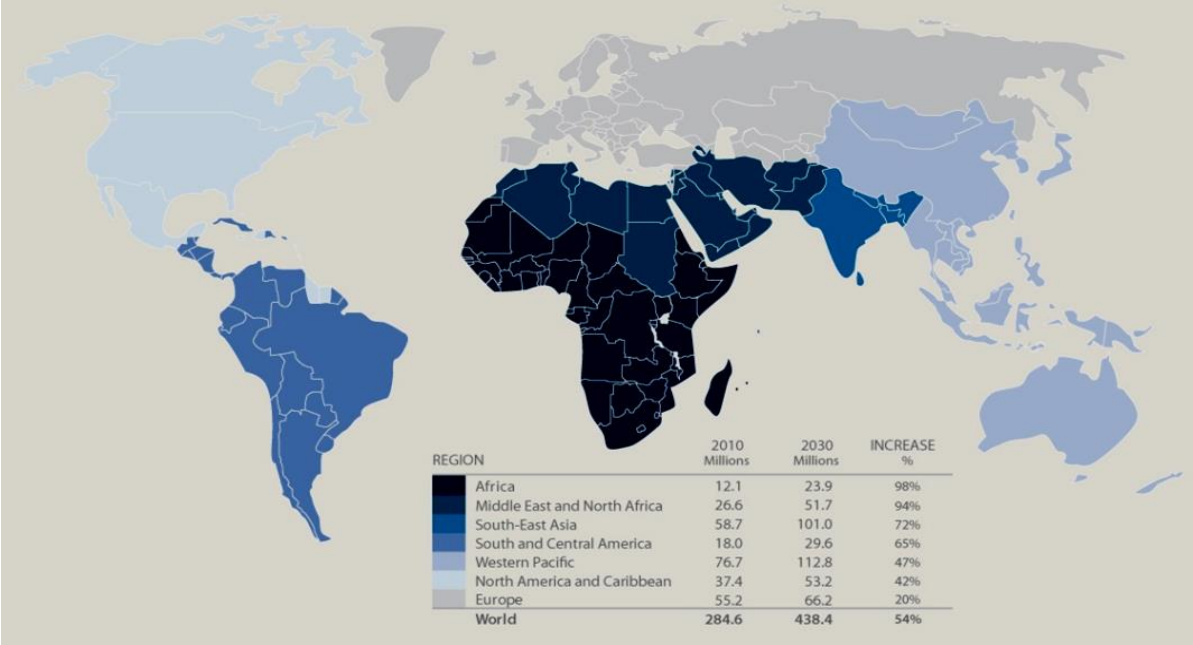


Figure 1 Global projections of the diabetes epidemic: 2010 - 2013 (millions). Modified from Reference 6. IDF Diabetes Atlas, 4th Edition, © International Diabetes Federation 2009

In UK, the number of people diagnosed with diabetes increased from 1.4 million in 1996 to 2.9 million in 2012. It is estimated that in the UK alone, there are 850,000 people who remain undiagnosed (Diabetes UK 2012). By 2024, it is expected that 5 million people will be living with diabetes. Type 2 diabetes accounts for around 90% of all cases of diabetes (IDF 2013).

1.4 **Diabetes mellitus**

The term diabetes describes a metabolic disorder, characterised by chronic hyperglycaemia and 'disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both' (WHO 1999). Chronic hyperglycaemia is associated with adverse outcomes: microvascular damage and an increased risk of macrovascular disease. Diabetes can be divided into 4 aetiological categories (Table 1) of which type 2 diabetes is the most prevalent and will be described in detail.

Table 1 Aetiological classification of disorders of glycaemia (modified from Alberti and Zimmet (1998))

Type 1	Beta cell destruction usually leading to absolute insulin deficiency. Autoimmune Idiopathic
Type 2	May range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with or without insulin resistance.
Other specific types	Genetic defects of beta cell function Genetic defects in insulin action Diseases of the exocrine pancreas (e.g. pancreatitis or cystic fibrosis) Endocrincopathies (e.g. Cushing's Syndrome) Drug or chemical induced Uncommon forms of immune-mediated diabetes Other genetic syndromes sometimes associated with diabetes (e.g. Down's Syndrome)
Gestational diabetes	Carbohydrate intolerance resulting in hyperglycaemia of variable severity with onset or first recognition during pregnancy. It has major implications for both foetus and mother and is a high risk factor for the development of type 2 diabetes.

Type 2 diabetes is characterised by relative (rather than absolute) insulin deficiency and peripheral insulin resistance. At the time of diagnosis, beta cell function is already reduced by around 50% and continues to decline regardless of type of therapy used. The main deficit in beta cell function in type 2 diabetes is the markedly reduced first and second phase insulin response to glucose, but the residual insulin secretion is sufficient to prevent lipolysis and ketogenesis. In most individuals insulin treatment is not required for survival but is increasingly necessary to achieve optimal glycaemic control and reduce the risk of complications.

1.5 **Diagnosis of diabetes**

The World Health Organisation (WHO) diagnostic criteria for diabetes are listed in Figure 2.

In the UK, a diagnosis of diabetes is made according to the WHO diagnostic criteria:

1. a random venous plasma glucose ≥11.1 mmol/L.
2. a fasting venous plasma glucose ≥7.0 mmol/L
3. a venous plasma glucose ≥11.1 mmol/L, 2 hours after a 75g load of glucose, the oral glucose tolerance test (OGTT)

Figure 2 The WHO diagnostic criteria for diabetes mellitus (WHO 1999)

Only one abnormal glucose value is required in a patient with diabetic symptoms, but a supplementary test is required in asymptomatic individuals. The most common symptoms are tiredness, malaise, polyuria, nocturia and thirst, and blurred vision may occur with rapid changes of glycaemia. Type 2 diabetes can remain undiagnosed for many years as hyperglycaemia, and is asymptomatic in up to 50% of cases. Diagnoses are often made through routine medical examinations and blood screening.

1.6 **The epidemiology of type 2 diabetes**

The causes of type 2 diabetes are multi-factorial and are predominantly genetic, environmental and behavioural (Alberti and Zimmet, 1998). Although genetic predisposition is an essential determinant of the development of type 2 diabetes, the activation of a genetic predisposition requires the presence of environmental and behavioural factors, many of which are associated with lifestyle. The most significant

risk factors are abdominal obesity and physical inactivity. Risk factors for type 2 diabetes can be categorised as modifiable or non-modifiable and are summarised in Table 2.

Table 2 An overview of the modifiable and non-modifiable risk factors for the development of type 2 diabetes

Genetic factors	Genetic markers e.g. 'thrifty gene(s)' Family history Ethnicity
Demographic characteristics	Increasing age
Behavioural and lifestyle-related risk factors	Obesity (including distribution of obesity and duration) Physical inactivity Diet Stress* Westernisation, urbanisation and modernisation*
Metabolic determinants and intermediate risk categories of type 2 diabetes	Impaired glucose tolerance* Insulin resistance* Gestational diabetes

* Risk factors on the causal pathway

1.6.i Non-modifiable risk factors

Genetics

Type 2 diabetes has a strong genetic basis and therefore typically clusters in families. First degree offspring have a lifetime risk of developing type 2 diabetes of 35% if one parent has type 2 diabetes and 70% if both parents have type 2 diabetes. A maternal history of diabetes confers a higher risk of type 2 diabetes than paternal history which may be explained by an effect of maternal hyperglycaemia during pregnancy. Ethnic differences in diabetes prevalence when exposed to the same environment also indicate a genetic predisposition. In the UK, the prevalence of diabetes in people of black or South Asian ethnicity is two- to four-fold higher than in adults of European

origin (Barnett et al. 2006, UKPDS 1994). These individuals also develop type 2 diabetes at a younger age than white British individuals (UKPDS 1994, Winkley et al. 2013).

Age

The prevalence of type 2 diabetes increases with age. Until recently, type 2 diabetes was considered a diagnosis of mid-life (>50 years of age), however the average age of onset is decreasing. There has been a shift in disease demography, with a worrying increase in the incidence of type 2 diabetes in young adults and adolescents. This rise is concurrent to the rise in obesity, sedentary lifestyles, poor diet and increase in fast food consumption.

Previous gestational diabetes

Gestational diabetes is more frequently seen in females at risk of developing type 2 diabetes, for example older, overweight or obese females from black or South Asian ethnic groups. Following delivery, glucose tolerance usually returns to normal, however women with gestational diabetes have a significantly higher risk of developing type 2 diabetes (Kim et al. 2002).

1.6.ii Modifiable risk factors

Obesity

Longitudinal evidence implicates obesity as the most powerful predictor of type 2 diabetes. Around 80% of people diagnosed with type 2 diabetes are overweight or obese. The risk of developing diabetes rises progressively with increases in body mass index (BMI) but studies suggest that measurements of visceral fat, such as waist circumference or waist-to-hip ratio, may be more strongly associated with the risk of developing type 2 diabetes. This indicates that the distribution of fat, rather than the total amount of fat, is more important. The accumulation of visceral fat, in particular, overexposes the liver to free fatty acids which results in insulin resistance and glucose intolerance and exacerbates metabolic abnormalities present in type 2 diabetes such as hyperinsulinemia, hyperglycaemia and dyslipidemia (Björntorp 1991).

Diet and physical inactivity

Diet and physical activity are risk factors for the development of type 2 diabetes, primarily through obesity. Consistent evidence suggests that high calorific and low fibre intake, high glycaemic load and a low polyunsaturated to saturated fat ratio may predispose type 2 diabetes, but there are still uncertainties surrounding dietary factors associated with the development of the disease, largely due to difficulties and inaccuracies in the measurement of dietary data (Hu et al 2001). Globally, energy intake is increasing, levels of physical activity are decreasing and in parallel, sedentary lifestyles are increasing. Physical inactivity is a major contributor to the obesity epidemic and is an independent predictor of type 2 diabetes in both cross-sectional and longitudinal studies (Hu et al. 2001).

Although genetic and lifestyle factors play a significant role, there are other potentially modifiable risk factors which may be implicated in the development of diabetes. This is demonstrated, most evidently, by global variations in morbidity and mortality rates according to socio-economic status. Significant drivers of these variations are social variables which describe the contexts in which we live. It is well known that disease is socially patterned, that is, disease prevalence varies across different societal groups.

The social gradient of type 2 diabetes is well established and a social patterning can be observed in its epidemiology. In most high-income countries, the prevalence of type 2 diabetes is inversely associated to socio-economic status. Within low- and middle-income countries this is reversed, with a higher prevalence of type 2 diabetes in those of high socio-economic status. However, in low-income countries, diabetes is increasingly prevalent in the urban poor (IDF 2012). Similar patterns were also seen in diseases that were regarded as 'diseases of affluence' in the early 20th century such as coronary heart disease, stomach ulceration, stroke and obesity. Over time, these diseases have become increasingly prevalent in the poorer sections of more affluent societies, reversing their social distribution (Wilkinson, 1996).

In addition to socio-economic determinants of type 2 diabetes, there are other, less frequently documented, social factors which may be implicated in the onset and progression of the disease. These factors are of primary interest to this thesis and include: social support, neighbourhood deprivation, obesogenic (obesity-promoting) environments, stressful life events, early life experiences and access to services (Gary-Webb et al. 2013).

1.7 **The management of type 2 diabetes**

Effective self-management is considered the cornerstone to achieving optimal glycaemic control to reduce the risk of developing long term diabetes' complications,

disability and death. In order to achieve optimal outcomes the National Institute for Health and Care Excellence (NICE) guidelines place emphasis on understanding diabetes, informed choices and the acquisition of the skills necessary for successful management (NICE 2008). Although delivery of these factors does not always take the form of clinical consultations, the guidelines still focus on the conventional medical model, with a nod to increasing recognition of psychological factors but with limited reference to individual social contexts.

1.7.iii Structured education

Structured diabetes education programmes should be made available to all individuals at the time of diagnosis. Several programmes have been developed in Europe and North America which are designed to achieve optimal outcomes through improving knowledge and skills, empowering individuals to take control of their diabetes, facilitating behaviour change and improving quality of life. The Diabetes Education and Self Management for Ongoing and Newly Diagnosed structured education programme used in the UK is one such example. The DESMOND programme offers 6 hours of self-management group education which is delivered by 2 healthcare professional educators over 1 day or 2 half-days. In a multi-centre clustered randomised controlled trial (RCT) in primary care, DESMOND was compared to usual care. Benefits of the intervention included weight loss, smoking status, a greater understanding of diabetes and lower depression scores at 12 months (Davies et al. 2008). HbA1c levels in the intervention group were lower than in the control group, but this association was not significant, this indicates that diabetes education alone may not be sufficient to significantly improve glycaemic control.

Diabetes education programmes acknowledge the social contexts of individuals as participants are given the option to bring a partner or friend to the sessions should they wish. From a patient perspective, the presence of a partner or friend in education

sessions may be supportive and empowering. It may also help the partner or friend to understand diabetes and the importance of self-management. However, results from previous studies are inconsistent. One frequently cited RCT comparing the effects of attending a 20-week behavioural weight control programme alone, or with a spouse, did not report significant differences in weight loss between groups post treatment or at 1 year follow-up. Moreover, the group attending sessions with spouses had greater attrition. There was a treatment and gender interaction. Females lost significantly more weight when treated with their spouses, but males lost more weight when treated alone (Wing et al. 1991).

1.7.iv Lifestyle modification

Individuals with type 2 diabetes should be supported to achieve optimal glycaemic control and reduce cardiovascular risk factors (BMI, blood pressure and cholesterol) by making modifications to lifestyle behaviours (diet, physical activity and smoking). Lifestyle modification, as a first line of treatment, generally appeals to individuals with newly diagnosed type 2 diabetes given the low risk and side-effects.

For patients, weight loss is the primary goal which is achieved through decreasing calorific intake and increasing energy expenditure. Within the multidisciplinary team it is common for a dietician to provide nutritional care and advice but the importance of healthy lifestyle management should be emphasised at all clinical contact. Dietary advice should address individual nutritional needs in accordance with personal choice, culture and willingness to change, but generally follows dietary advice for the general population (NICE 2008).

The management of obesity or smoking are not specifically addressed in relation to individuals with type 2 diabetes but also follow advice for the general population (NICE

2008). Adults should aim to engage in 150 minutes of physical activity per week, muscle strengthening exercises on 2 days per week and minimise sedentary time (Department of Health 2011). Smoking cessation should be actively encouraged. Except in exceptional circumstances, all smokers should be advised to quit and cessation advice can be based around existing medical conditions, if applicable (NICE 2008).

Diabetes self-care regimens are complex and patients frequently report difficulties in adherence. Adherence is defined by the WHO as 'the extent to which a person's behaviour – taking medication, following a diet, and / or executing lifestyle changes – corresponds with agreed recommendations from a healthcare provider' (WHO 2003). Non-adherence may occur as a result of biological, psychological and social circumstances, for example, physical disability, low self-esteem and social isolation respectively and can be categorised as i) intentional (the patient decides not to follow treatment recommendations) or ii) unintentional (the patient has practical difficulties in following treatment recommendations). According to the WHO definition, adherence is focused on behavioural factors, the understanding of which are underpinned by psychological and social constructs which may be beyond the scope of the current biomedical model of care used in diabetes.

For the most part, the self-management of type 2 diabetes takes place within social contexts which may facilitate or pose barriers to the required lifestyle changes. Lifestyle management may alter family and social routines but, ideally, supportive social contacts may assist and encourage healthy lifestyles, provide advice and guidance and reduce a sense of isolation. In a recent study of 13,366 individuals with type 2 diabetes in Northern California, emotional support and social connectedness were significantly associated with adherence to lifestyle modifications: diet, physical activity and foot checks (Rosland et al. 2014). An individual's residential neighbourhood may also have implications for leading healthy lifestyles. Self-management may be facilitated by living in neighbourhoods supportive to healthy

lifestyles (access to exercise facilities and healthy food). For example, living in safe neighbourhoods with access to green space may encourage walking or other forms of physical activity.

1.7.v Oral antidiabetic agents

When diet and exercise alone fail to optimise glycaemic control, antidiabetic agents are required in addition to lifestyle management. There are four main categories of oral agents: 1) insulin secretagogues (sulphonylureas), 2) insulin sensitisers (metformin and thiazolidinediones), 3) inhibitors of glucose absorption from the gastro intestinal tract (alpha-glycosidase inhibitor) and 4) incretin based therapies. Drugs from different categories can be combined with disease progression. The NICE guidelines (2008) recommend metformin as the first-line for glucose-lowering therapy. If an individual does not tolerate metformin and is not overweight, a sulfonylurea may be considered instead. A sulfonylurea may also be initiated if a rapid response is required due to hyperglycaemic symptoms. They may also be considered as second-line therapy, in addition to metformin, if glucose control remains inadequate (NICE 2008).

Individuals with type 2 diabetes often have difficulties adhering to medication regimens. NICE estimates that between a third and a half of medication prescribed for long term conditions are not used as recommended. This does not only represent a health concern but also an economic loss for society. The first step in improving medication adherence is to understand factors associated with non-adherence and to learn how to support adherence. In type 2 diabetes, one of the main reasons for intentional non-adherence to oral medication is the associated side-effects. For example, metformin is associated with nausea and gastro-intestinal discomfort which may not be tolerated by patients. Reasons for unintentional non-adherence may include cognitive impairment, emotional stress, confusion or competing familial demands and responsibilities. The social environment may play an important role in

unintentional non-adherence. For example, family and friends may promote patient adherence by providing psychological support, increasing self-esteem, encouraging optimism and buffering the stresses of being ill. They may also provide practical assistance, such as collecting medication, providing reminders or crushing or dissolving tablets if necessary.

Interestingly, in long term conditions, social support is less frequently associated with 'medical' self-care behaviours such as blood glucose monitoring or medication adherence (Gallant 2003, Rosland et al. 2014). This may reflect a lack of knowledge, ability or confidence of friends and family when formal training may not have been received.

1.7.vi Insulin treatment

With disease progression, many people with type 2 diabetes require insulin treatment which is frequently used in combination with oral antidiabetic agents, most commonly metformin. Using metformin in conjunction with insulin can reduce the number and severity of hypoglycaemic episodes and weight gain associated with insulin therapy.

The aim of insulin treatment is to mimic the daily fluctuations of insulin concentrations in healthy individuals as closely as possible. Insulin therapies are tailored to meet individual requirements to achieve optimal control without the risk of hypoglycaemia. Insulin is the most effective glucose lowering agent, but despite this, non-adherence is high which poses significant problems in clinical care. Insulin treatment is often resisted and its side-effects (hypoglycaemia and weight gain) feared. As a consequence, insulin treatment is perceived to be a 'last-resort' amongst patients and some practitioners. Insulin therapy may carry a sense of personal failure, shame and stigma for certain individuals. Reluctance to use an injectable drug, needle phobia, fear and embarrassment have also been cited as further barriers to insulin use. Results from the cross-national Diabetes Attitudes, Wishes and Needs (DAWN) Study of

individuals with type 1 and type 2 diabetes reported that insulin omission was independently associated with older age, lower income and education, type 2 diabetes, poor diet adherence, more frequently prescribed injections, interference with daily activities, pain and embarrassment (Peyrot et al. 2005).

Social contacts could provide the support necessary to overcome social barriers, lessen anxiety and facilitate insulin adherence. In the adolescent type 1 diabetes literature, family support typically provides tangible assistance for self-management tasks such as monitoring blood glucose and administering insulin. This may also be the case for individuals who are unable to administer their own insulin. Although social support in type 2 diabetes is less commonly associated with 'medical' self-management behaviours, for individuals who fear insulin regimen, living with others may provide psychological support and lessen the concern associated with adverse side-effects, such as hypoglycaemia. On the other hand, people on insulin therapy typically receive more support from healthcare professionals than those treated with oral medication so the influence of family and friends may be less important.

The current guidelines do not address, to any significant extent, social factors which may influence the self-management of diabetes. This is despite the National Health Service (NHS Choices) and Social Care Model acknowledging that the care of chronic disease should be multi-dimensional (linking health, social care, patients and carers) and multi-disciplinary. In one of very few instances, the NICE guidelines document that, if the patient agrees, the families and carers of individuals with type 2 diabetes should be given the opportunity to be involved in decisions regarding treatment (NICE 2008). The NHS also states that in long term conditions, patients with 'self-care support' can experience less pain, anxiety, depression and have a better quality of life (NHS Choices 2012). However, the extent to which healthcare professionals are mobilising carer support in diabetes management is unknown. In the conventional medical model of care, there is an emphasis on support from healthcare professionals, rather than support from family members or friends, but healthcare systems often do

not have adequate resources to provide support to individuals. Given the complex nature of self-management, time limited appointments may not be sufficient to address all of an individual's needs. Support from 'readily available' social networks such as family and friends may provide alternative supportive resources. Furthermore, neighbourhood environments are given limited consideration but are increasingly recognised by policy makers. Living in neighbourhoods conducive to the management of diabetes may be instrumental to optimal outcomes. Areas that are not supportive to the lifestyle changes that diabetes necessitates (unsafe neighbourhoods with high levels of crime, lack of exercise facilities and open green spaces and access to energy dense fast food outlets) may negatively influence an individual's likelihood of successfully managing the disease. As a result, it is important for healthcare professionals to understand their patients' social contexts when evaluating the effectiveness of different behaviour change interventions.

1.8 **Complications of diabetes**

The sub-optimal management of type 2 diabetes and sustained hyperglycaemia predisposes accelerated development of diabetes associated complications, reduced quality of life, disability and premature mortality. The complications of diabetes can be broadly categorised as microvascular and macrovascular.

Microvascular complications affect the small blood vessels in the eyes, kidneys and nerves. This leads to an increased risk of retinopathy, nephropathy and neuropathy, respectively, which ultimately affect over 80% of individuals with diabetes. In the US, almost 60% of individuals with type 2 diabetes will develop diabetic retinopathy (ADA 2002) and risk for neuropathy is estimated to be 20%. Lower limb amputation is 15 times higher in individuals with type 2 diabetes when compared to the general population.

Macrovascular disease damages the larger blood vessels affecting blood supply to the heart, brain, legs and feet. This leads to an increased risk of coronary heart disease, myocardial infarction (MI), cerebrovascular disease and peripheral vascular disease. In Europe, macrovascular disease is the main cause of death in individuals with type 2 diabetes (Laing et al. 2003). Compared to the general population, coronary and cerebrovascular disease is at least 50% more prevalent in people with type 2 diabetes (Morrish et al. 2001). Diabetes is the leading cause of adult blindness, renal failure, non-traumatic amputation and cardiovascular disease.

Although the complications of diabetes are ultimately irreversible, their progression can be slowed with good glycaemic control alongside treatment of known cardiovascular risk factors such as hyperlipidaemia and hypertension. Results from the UK Prospective Diabetes Study (UKPDS), a landmark randomised multi-centre trial of 5,102 participants with newly diagnosed type 2 diabetes, reported that with intensive reductions in HbA1c over the first 10 years of diagnosis, the risk of diabetes complications also reduced. Patients in an intensive treatment group demonstrated a 25% reduction in microvascular complications (Turner et al. 1998). The risk of macrovascular complications did not differ significantly between intensive therapy and conventional treatment groups, although there was a 16% (non-significant) risk reduction in myocardial infarction in the group receiving intensive treatment. Similarly, in the Steno-2 RCT of 160 high risk participants with type 2 diabetes and microalbuminuria, an intensive intervention with multiple drug combinations and behaviour modification was associated with a risk reduction of 20% of death from any cause over a 13.3 year follow-up period. The absolute risk of death from cardiovascular disease was also reduced by 13% in the intensive therapy group (Gæde et al. 2008).

1.9 **Costs of diabetes**

In addition to immense human suffering, diabetes accounts for a disproportionate use of health service expenditure. In 2011, the cost of diabetes to the NHS was £10 billion, or £1 million per hour (Hex et al. 2012). This figure is expected to rise to £16.9 billion by 2035. Ten per cent of the NHS budget is spent on diabetes and its complications and around 80% of this is used to manage potentially preventable complications (Department of Health 2006). Almost 90% of costs are associated with type 2 diabetes (Hex et al. 2012).

There are also indirect costs of the disease. These include social and productivity costs which are borne by all of society; patients themselves, carers, employers, social security and benefit payments. In 2011, the indirect costs of diabetes were £13.9 billion. By 2035 this is estimated to be £22.9 billion (Hex et al. 2012).

The rising costs of diabetes further necessitate the identification of alternative and cheaper modifiable targets of intervention beyond the medical model. Social factors may be one such target of intervention. Social factors have been identified as important prognostic variables across a range of conditions but their role in type 2 diabetes remains inconclusive. I have described a potentially important role of social factors in the course of type 2 diabetes and for the remainder of this chapter I will introduce the theoretical basis of the social determinants of health before proposing an epidemiological model of the social determinants of glycaemic control in type 2 diabetes.

1.10 **The social determinants of health**

The latter half of the 20th century has seen a shift in the focus of attention from the biological causes of disease to include other possible determinants, such as social and psychological constructs. Social factors are now accepted as plausible and important influences of morbidity and mortality (Figure 3) and as such, have gained increasing emphasis in both health and mental health research and are now reflected in commissioning priorities (Marmot 2005). Biological expressions of social inequality are core concepts in social epidemiological research (Krieger 2001). The implication this holds is that health can be regarded as a social as well as a medical concept.

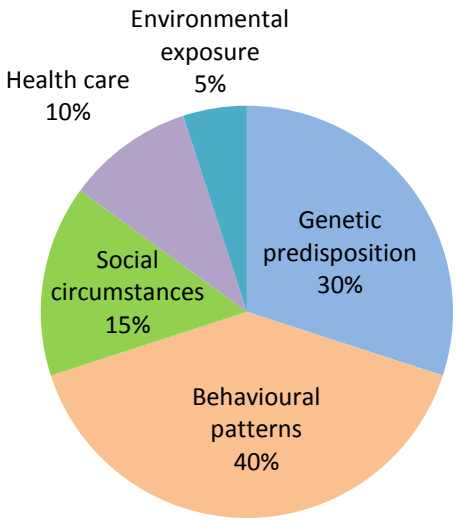


Figure 3 Proportional contribution to premature death (Schroeder 2007)

Social determinants exert a significant influence on health outcomes and are important contributors to health inequalities (differences in health status or in the distribution of health determinants between different population groups). National policy recognises that 'material circumstance, social environment, psychosocial factors, behaviours and biological factors are all important influences on health' (Department of Health 2010). In the recent World Health Organisation Commission on Social Determinants of Health, Professor Michael Marmot described social determinants of health as social and physical factors 'which impact upon health and

well-being: the circumstances in to which we are born we grow, work, live and age' (CSDH 2008). These factors are illustrated by the widely cited theoretical 'rainbow' of the social determinants of health by Dahlgren and Whitehead (2007)(Figure 4) and are the driving force behind health inequities.

To tackle increasing inequalities, on a national and global scale, it is important to consider the much broader context of our lives. Whilst globally, life expectancy is increasing, there exists significant variation in health status and well-being in different population settings. There is a clear social gradient in health: the more adverse the social conditions, the worse an individual's health. Such disadvantaged individuals are likely to have a greater burden of ill health and shorter life expectancy.

Social factors are described as the 'causes of the causes' of ill health. At the launch of the CSDH Final Report in Geneva in 2008, Dr Margaret Chan, the Director General of the WHO said "*health care is an important determinant of health. Lifestyles are important determinants of health. But it is factors in the social environment that determine access to health services and influence lifestyle choices in the first place*." It is these factors that need to be understood to guide successful interventions for behaviour change amongst individuals and communities with the poorest health. Focusing intervention and resources on downstream proximate measures of health inequalities are at best not likely to reduce health inequalities, and at worst likely to increase disparities. The quote from Dr Chan highlights the need to study the determinants of conventional risk factors in health: the *causes of the causes* of poor health.

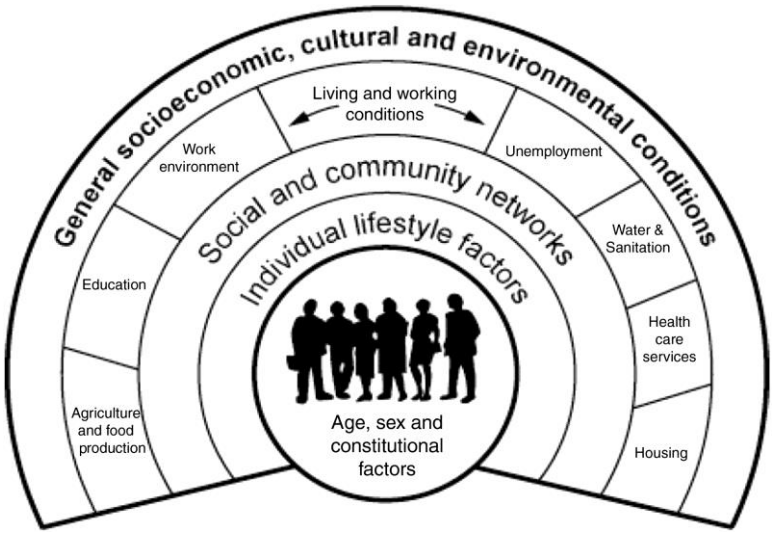


Figure 4 The social determinants of health (Dahlgren and Whitehead 2007)

This thesis will focus on two components or 'layers' of the social determinants of health rainbow: i) social and community networks (social support) and ii) neighbourhood environment. These determinants are hypothesised to be important in the (self-) management of type 2 diabetes. As previously described, social support is associated with health outcomes and may be particularly important in type 2 diabetes, a disease which requires the active management of the individual. Having a supportive family, social network and community may help with the management of a disease and reduce the associated burden. Obesogenic environments and unsafe environments, not conductive to leading a healthy lifestyle, play a large role in the social patterning of diabetes.

1.11 **Proposed model**

Although Dahlgren and Whitehead provide a useful theoretical framework (Figure 4) for the social determinants of health, it is less useful as an epidemiological model. I propose and present a theoretical framework for the determinants of glycaemic control in type 2 diabetes (Figure 5) and aim to establish a testable epidemiological model for this association (Figure 6).

Figure 5 describes the importance of a bio-psycho-social approach in type 2 diabetes and the interacting nature of these dimensions. This conceptual framework utilises a multilevel socio-ecological approach and expands upon the narrow emphasis on individual or behavioural factors and considers the society within which we are embedded. Although not graphically displayed, it is recognised that factors at a local or national governmental level (for example, policy) and at organisational levels (for example, the provision of local health care services) may influence the association between biological, psychological or social factors and glycaemic control.

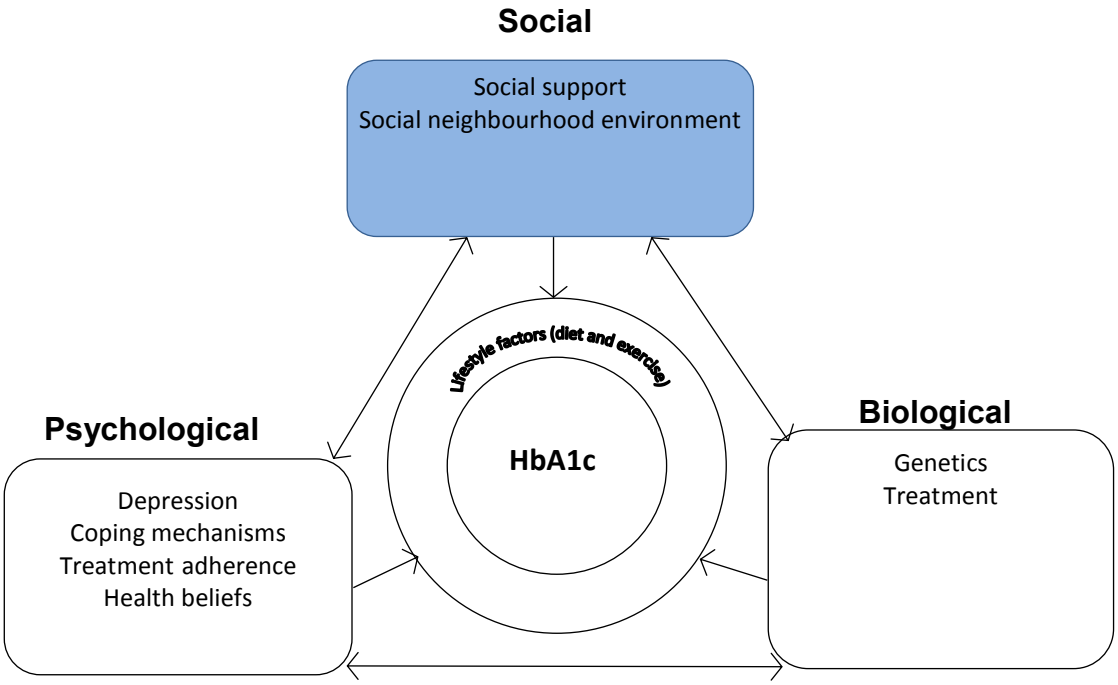


Figure 5 The theoretical framework for the determinants of glycaemic control in type 2 diabetes

Figure 6 focuses on the social dimension of Figure 5 (the highlighted box). It describes the social factors that are used in this thesis at the individual and area level and broadly demonstrates the associations under investigation.

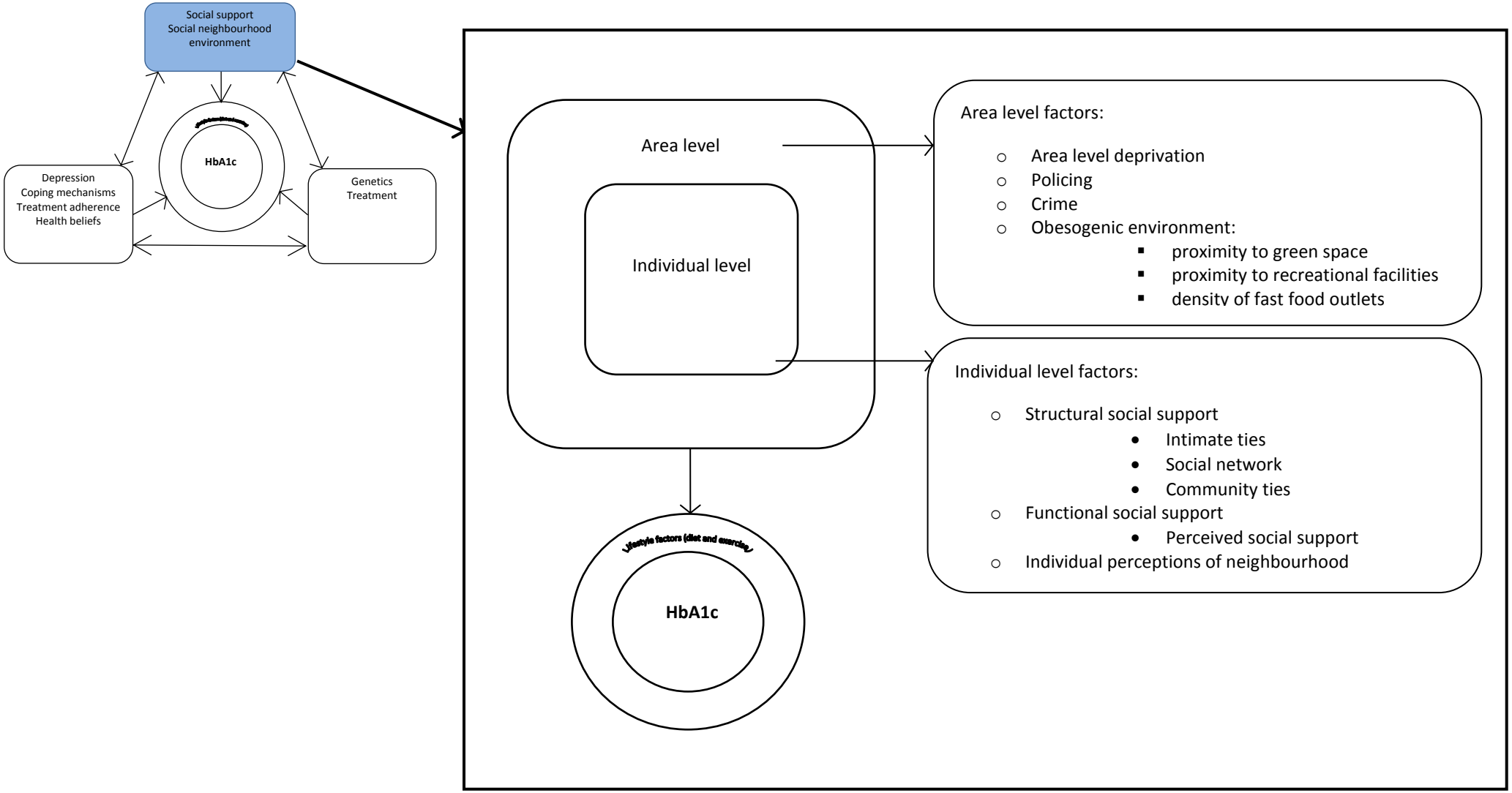


Figure 6 A proposed epidemiological model of the social determinants of HbA1c in type 2 diabetes

1.12 **Other social factors**

There are already many social factors recognised as contributors to health inequalities and some of these will be omitted as main explanatory variables in this thesis. Primary reasons for the selective inclusion of independent variables were to i) comprehensively study two social constructs; ii) limit variables in multivariable analyses and iii) reduce the possibility of colinearity. Furthermore, some variables, such as socio-economic status, are established predictors of adverse health outcomes and were not included for this reason.

Individual socio-economic status is not used as a main explanatory variable, but will be retained as a confounder in statistical analyses. An extensive body of literature associates socio-economic status, morbidity and mortality across a range of acute and chronic disease (Marmot et al. 1987, Ramsay et al. 2011). In diabetes, socio-economic status is associated with the onset, course and outcome of the disease (Connolly et al. 2000, Bihan et al. 2005). Other factors, which are related to socio-economic status, will also not be considered. These include: illiteracy, poor social housing and overcrowding but will be captured in overlapping measures of deprivation.

Social factors such as stigma and racism are complex to study, measure and quantify and are beyond the scope of this thesis which is predominantly epidemiological with a focus on generic social processes applicable to all populations. However, ethnicity will be used as a covariate in analyses and stratified where appropriate.

There are also important determinants of health at central and local government levels and at the level of healthcare providers. Characteristics of healthcare settings such as number of doctors, diabetes specialist care and the provision of diabetes education may also be associated with biomedical outcomes. In this thesis, analyses accounts for clustering within GP practices reflecting variations in service provision, but data on the specific services provided by each practice were not routinely collected.

1.13 **Conclusions**

The increase in the prevalence of type 2 diabetes highlights the need to further understand factors associated with its onset and course. There is an increasing need to identify determinants beyond established risk factors such as obesity and sedentary behaviour (Agardh et al. 2011). Increasingly, evidence is suggesting that social determinants may play an important role in the management of type 2 diabetes.

The next chapter will describe the concept of one of the social determinants to be studied, social support, and its association with health outcomes.

Chapter 2 Social Support

2.1 **Synopsis**

This chapter describes the first social construct under study, that is, social support (Figure 7). Social support is recognised as an important prognostic variable for health and has undergone much scrutiny in research. This chapter gives a theoretical overview of social support and synthesizes the evidence of an association between social support and biomedical outcomes, morbidity and mortality. The proposed mechanistic routes of action are also discussed.

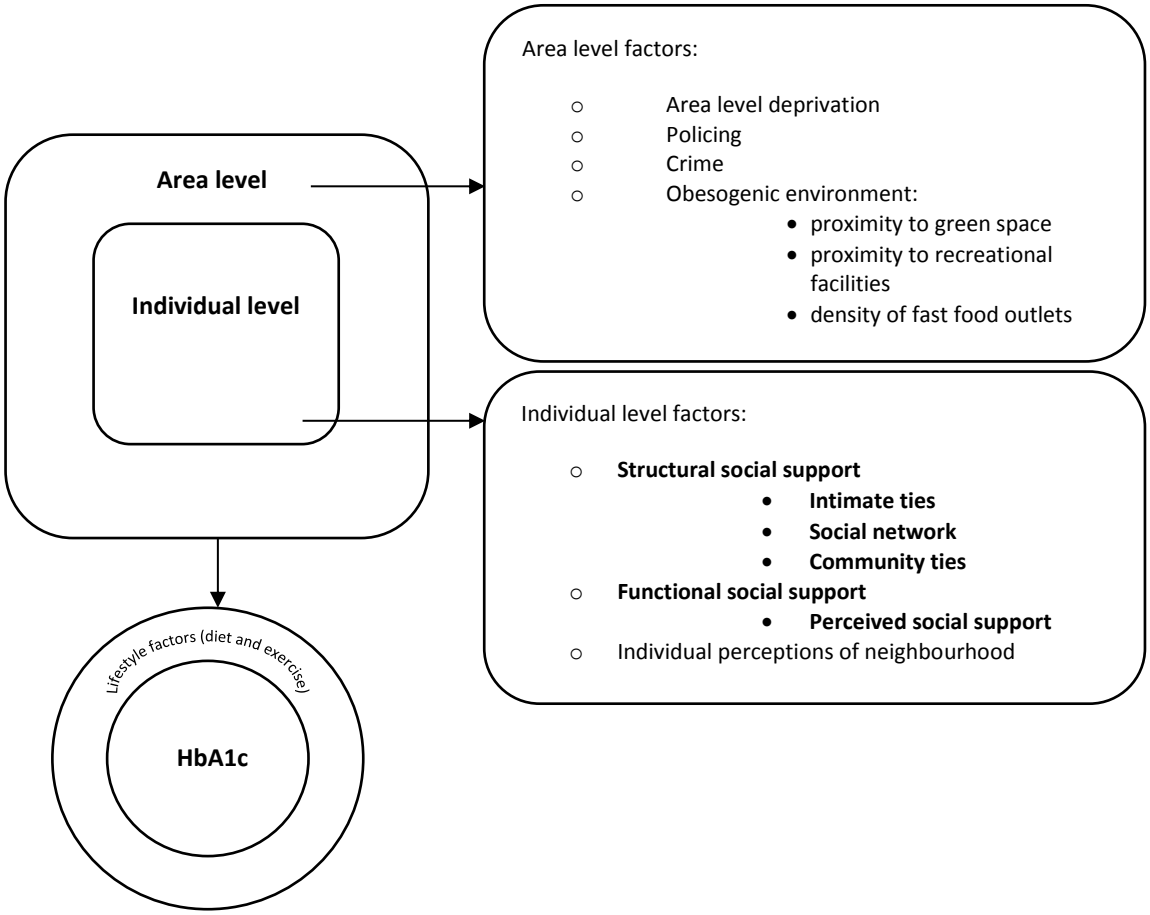


Figure 7 The proposed epidemiological model of the social determinants of HbA1c in type 2 diabetes (the variables under study in this chapter are highlighted)

2.2 **Introduction**

The past three decades have witnessed the emergence of the concept of social support as an important factor in health (Cohen 2004, Uchino 2006). Social support has been well studied as a risk factor for poor health in health promotion research (Gleeson-Kreig 2008) and has been a target for intervention in many health conditions (van Dam et al. 2005). The literature consistently reports that individuals who are socially integrated have a lower risk of premature all-cause mortality than individuals who are socially isolated (House 2002, Berkman 1995, Berkman and Syme 1979, Holt-Lunstad et al. 2010). A recent meta-analysis of 148 prospective studies indicates that people with stronger social relationships have a 50% increased likelihood of survival (Holt-Lunstad et al. 2010). The association between social relationships and mortality is comparable to established risk factors such as smoking and greater than obesity and physical activity (Holt-Lunstad et al. 2010). Not only the quantity, but also the quality of social support have been repeatedly associated with morbidity and mortality in a number of chronic health conditions (Berkman 1995, Berkman et al. 1992, Orth-Gomér 2009). In epidemiological research, social support is associated with a more favourable 'biological profile' across a number of diseases (Uchino 2006).

The earliest theories of the association between society and health were proposed by the French sociologist Emile Durkheim who was one of the first to describe a link between social integration and mortality and the protective functions of being part of a social group or community (Durkheim 1897). He developed this in his book, *Suicide*, where Durkheim described the social underpinnings of suicide. He argued that 'social facts', particularly levels of social integration, can be used to explain the social patterning of suicide rates. Durkheim's theories also related to other major outcomes such as homicide, violence and cardiovascular disease.

The early concepts of social support were understood in terms of socio-economic status indicating social class and social standing. More recently, social support has

come to represent an umbrella term for a number of related constructs, broadly classified as i) structural and ii) functional social support (Figure 8). Whilst it is acknowledged that socio-economic status plays an important role in buffering distress, thinking about social support in terms of its structural basis offers a more cohesive and coherent theoretical platform on which to understand the component parts of social support. Support structures offer a basis from which functional elements of social support emerge (annotated by the dashed arrow in Figure 8).

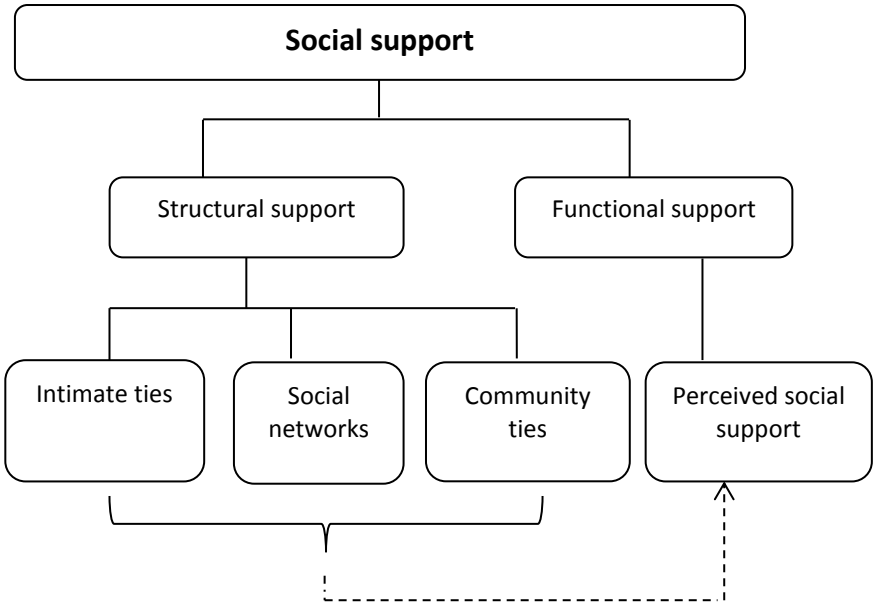


Figure 8 The component parts of social support

A further distinction can be made between formal and informal social support. Formal support refers to narrowly defined support provided by a bureaucratic system. Such support might be task orientated, paid and involve the application of professional knowledge and skills and provided by a nurse or other social care provider. Informal support on the other hand, is much more flexible, free, readily available and responsive to individual needs. Informal social support may be provided by a spouse or a close friend and represent a more constant source of support. An informal source of support might help with every-day tasks whereas formal social support may only be available by appointment and may be constrained by time. The constructs of social support in this thesis are informal. They were chosen because the majority of self-

management for long term conditions takes place in the home and formal healthcare settings play a relatively small role. Informal social networks may therefore form an integral component of the management of long term conditions.

Despite a long history of the beneficial effect of social support on both physical and psychological well-being, methodological issues have hampered the progression of this theme. In the social support literature, three main areas of contention exist: i) how to define social support; ii) how to measure social support and iii) the mechanisms by which social support influences health outcomes. These issues are interrelated; the way in which social support is measured and conceptually understood undoubtedly reflects how it is defined. Although there is no single accepted definition of social support (Uchino 2006), it is a multidimensional concept that can broadly be defined as: '*information from others that one is loved and cared for, esteemed and valued, and part of a network of communication and mutual obligations from parents, a spouse or loved one, other relatives, friends, social and community contacts such as churches or clubs*' (Siegel 1993).

2.3 **Structural support**

Human relations consist of multiple social bonds which form layers extending from the individual (Lin et al. 1999). These layers can be classified as intimate relations, social networks and community ties (Figure 9). Within the inner layer, intimate relations, strong emotional ties and binding relationships exist. Strong ties are constructed by the sharing of confiding information and mutual trust. This type of relationship would typically be shared with a spouse or partner. Marital status is the most commonly used marker of intimate ties. The middle layer consists of the social network of an individual which requires more effort than simple participation. It requires interpersonal interactions which in turn maintain the social networks. Friends, family and colleagues may typically constitute an individual's social network but regular contact with professionals such as healthcare providers or social services would also be included.

The outer layer, community ties, provides a sense of belongingness and social identity, without relying on, or requiring actual person to person interaction. Community ties reflect the extent to which individuals participate and immerse themselves in the community. This type of social support may be provided by religious, recreational or civic groups. The most frequent measure of social networks and community ties is the quantitative assessment of networks or ties, simply, a count of network members reported by an individual. Here, no information about the nature of the social relationship is recorded.

The extent of structural embededness is characterised by these three layers of structural support. An individual's location within each layer of the structure determines the likelihood of accessing social support in times of need.

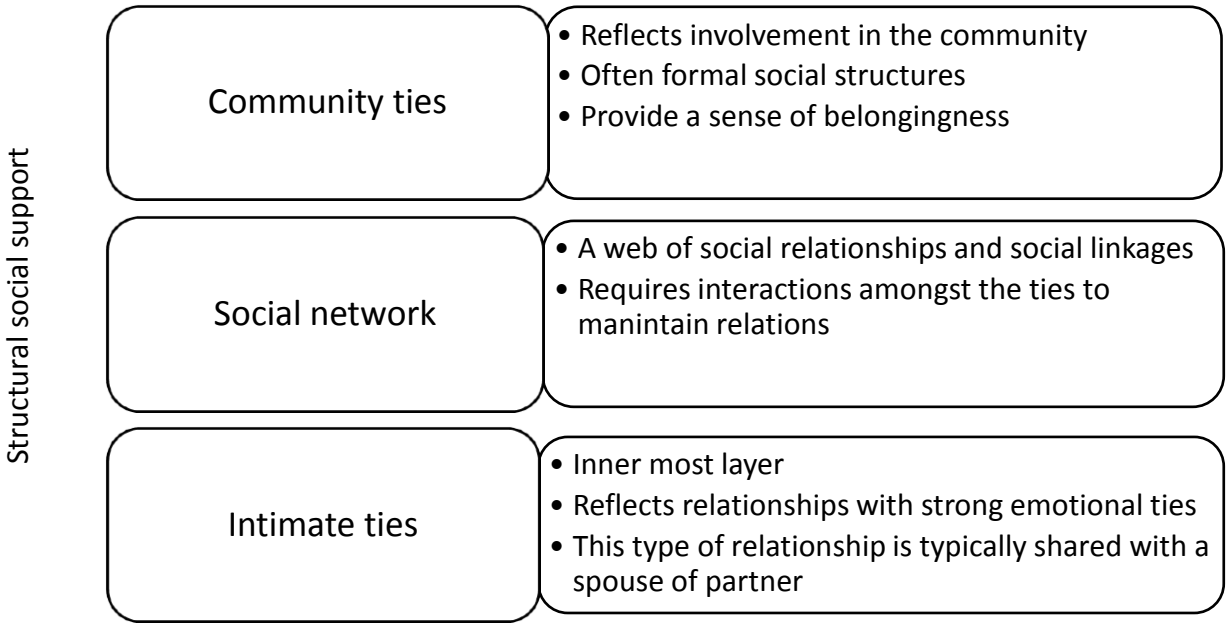


Figure 9 The 3 layers of structural social support

2.4 **Functional support**

The functional aspects of social support primarily include actions that are defined by the needs they serve; emotional, informational, tangible (concrete assistance; for example, financial, material or the provision of services) or perceived social support. Functional support differs from structural support. The former describes the (perceived) utility and functionality of intimate support, social networks and community ties and the latter describes the existence of social contacts (Smith and Christakis 2008). Another important component is the quality of social support. The structural dimensions of social support do not typically reflect the quality of support, they only increase the likelihood of receiving social support when required. Functional support however, particularly the perception of functional support, reflects the quality of support provided but these constructs are often distinguished for the purpose of analysis.

This thesis will predominantly focus on perceived social support. Perceived social support refers to the perceptions of availability of support when it is needed. Research has shown that, in general, perceived social support is a more effective component of resisting distress than actual social support (Uchino 2009). This indicates that the belief that support is available buffers the impact of potential stressors more effectively than the knowledge that support has previously been received for these stressors.

2.5 **Structural social support and health**

2.5.i Intimate ties

Intimate ties are characterised by emotional and/or physical intimacy and mutually confiding relationships. This type of relationship is typically shared with a spouse or a partner. Historically, social support was defined according to marital status (Wilcox 1981). Whilst the definition of social support has evolved, marital status is the most

commonly used marker of presence of an intimate tie. Being married often implies that social support is readily available and spouses and partners are most frequently named as the primary source of support (Revenson 1994, August and Sorkin 2010).

Marriage, the union of two individuals, is suggested to offer a protective effect for health outcomes. This includes social, emotional and instrumental support, better regulation of health related behaviours and economic benefits, which may be particularly relevant to women in older cohorts. Epidemiological research consistently reports an association between marriage and lower incidence of health problems and reduced mortality when compared to unmarried individuals (Johnson et al. 2000, Berkman et al. 2000, Cohen 2004). This association is observed across a number of health conditions including cancer, cardiovascular disease, recovery from surgery and the management of chronic disease (House et al. 1988). Being married has a significant effect on survival rates following coronary artery bypass grafting (CABG); married individuals were 2.5 times more likely to be alive 15 years after CABG (King and Reis 2012). They also have lower mortality rates than single, divorced and widowed people (Verbrugge 1979), report greater life satisfaction, happiness and have a lower risk of depression (Gove et al. 1983). Unmarried people, particularly those who have never been married, have a higher risk of dying from chronic or acute cardiovascular disease (Sorlie et al. 2004). Cohabitation is increasingly commonplace and whilst older studies may not have taken this into account, it is speculated that cohabiting individuals might also benefit from the same protective effect as married individuals although whether it provides the same stability as marriage is not known.

However, the association between marriage and good health is not universal. Marriage may also have negative effects on physical and mental health (Ortega et al. 2011). The interdependence of two people can be detrimental for health status, for example, the hospitalisation of one spouse has been shown to increase the risk of death in the other (Christakis and Allison 2006). Furthermore marital relationships are not always supportive and it seems that close social relations must also have a certain quality.

Poor quality relationships may have a negative effect on health outcomes (Kiecolt-Glaser and Newton 2001), as such, single individuals are reported to have better health status compared to those who are unhappily married (Holt-Lundstad 2008). Non-supportive behaviour such as nagging and criticism can reduce individuals' sense of autonomy with the potential to render them less motivated to cope with the burden of chronic disease and adhere to self-care regimens (Clark and Nothwehr 1997, Boehm et al. 1997).

The construct of marriage has a number of components and is more complex than it initially appears. It is an aggregate measure of intimacy, a confidante, emotional support and practical assistance but also overdependence, a source of conflict or burden. It appears that marriage per se is not universally beneficial, rather the quality and satisfaction of the marriage. With changes in attitudes towards marriage and increase in cohabitation, particularly in the Western world, the effect on health remains to be seen.

2.5.ii Social networks

Social networks characterise the web of social relations surrounding an individual. The sum of one's social network or personal ties is a social resource on which one can draw in times of difficulty or stress. Social network integration is associated with positive psychological states, recognition of self-worth and a sense of belonging and security (Sheldon Cohen et al. 2000). Having a large social network does not necessarily increase the amount of social support received, but it undoubtedly increases the probability of receiving it. Social networks vary across the life course and according to factors such as gender, ethnicity, employment status and depression status (Uchino 2009).

A lack of social network, characterised by social isolation and few social relations, is associated with higher rates of overall mortality (Orth-Gomér 2009, Holt-Lunstad et al. 2010). Large social network size has been associated with longevity, reduced cognitive decline, reduced susceptibility to infectious disease and better prognoses in life threatening conditions (Cohen and Janicki-Deverts 2009). Social networks have consistently been implicated as an important prognostic variable for future macrovascular events in cross-sectional and longitudinal studies. In a cross-sectional study of 783 participants, individuals with smaller social networks had an elevated risk of coronary artery calcification even after adjustment for age, gender, systolic blood pressure, blood glucose and low-density lipoprotein. A similar finding was seen in a longitudinal study (median 5.9 years follow-up) in females at high risk of cardiovascular disease, those with smaller, less diverse social networks were more than two times as likely to experience a stroke, independent of demographic variables, depression and biological risk factors (Rutledge et al. 2008).

Social networks can also have unintentional negative influences on health outcomes (Gallant 2003). The influence of peers and close social contacts can manifest in social pressure, social comparison and behaviour approximation which may result in health behaviours spreading through social networks. Consistent findings suggest that the body weight of friends are highly correlated and a person's chances of becoming obese during a specified time period is partially determined by whether or not members of their social network also become obese during the same time frame (Christakis and Fowler 2007). Network members can promote unfavourable health behaviours and set a negative example for the management of chronic conditions. Smoking and drinking, for example, may be commonplace within certain social networks and regarded as a social norm (Smith and Christakis 2008).

2.5.iii Community ties

The community of an individual provides a sense of belonging, a feeling of membership and connectedness (Block 2008) and provides an individual with a sense of identity. Community ties and organisations are proposed to bring about beneficial effects on health status in three ways: i) material benefits, for example, wages or information, ii) solidary benefits, such as socialising and group identification, and iii) purposive benefits such as fulfilling a sense of one's responsibility and bettering the community (Prestby et al. 1990).

Community ties differ from social networks in that they are more formal social structures, with members often working towards shared ventures and where dense networks of civic participation exist. Participating in group recreation, church attendance or holding occupational or social roles are all instances of engagement with the community. It is speculated that community participation based on shared work experiences (for example trade unions), health experiences (for example a diabetes support group), religious affiliations (for example a church) or a neighbourhood group (for example Neighbourhood Watch) provide access to resources which have direct and indirect effects on health outcomes. Being a member of such groups, clubs or organisations has been shown to positively influence the health of a community (MacIntyre et al. 1993), but less research has focused on the effects on the individual.

At an area level, in a cross-sectional study across 39 states in the US, increased membership of voluntary organisations per capita was associated with a decrease in mortality rates. This association was independent of area level socio-economic status which was measured using the revised federal poverty index which is based on wage-income and does not reflect receipt of state benefits (Kawachi et al. 1997). In Scotland, local association membership at the area level, matched to participant postcodes, was

independently and positively associated with self-rated health status (MacIntyre et al. 1993).

Findings at an individual level are less consistent. Most commonly reported are the beneficial effects of religious organisation affiliation, which is associated with reduced morbidity and longevity (Chatters 2000) but less research has been done to investigate the association between community involvement and health. In a cross-sectional study of a US community sample in 1984 (Rietschlin 1998), voluntary group members reported lower levels of depressive symptoms in the presence of stressors than those who were not members of a voluntary group. This association was independent of demographic and socio-economic variables. Although a large evidence base is lacking, these findings may be particularly pertinent to older people and to individuals whose health is compromised. As people age, they are significantly disadvantaged in maintaining and strengthening social ties, due to retirement, disability or death of a spouse or friends. However, this effect is not observed in formal organizations such as community ties which are more permanent sources of structural support that do not diminish with age (Young and Glasgow 1998). For example, a voluntary art group will continue to function each week regardless of age, sickness or weekly absences.

2.6 **Functional social support and health**

The functional aspects of social support are defined by the needs they serve and the perception of the quality of support received.

2.6.iv Perceived social support

The most striking associations between social support and health status come from social integration research which uses quantitative data concerning the size of an

individual's social network. However, despite less research, the functional components of social support might be equally important. The perception of existence of help and assistance from others (perceived social support) protects against daily life stresses (Cohen 2004). It is important to investigate structural components (social networks and community ties) independently of functional support, as structural measures may reflect, but are not always associated with, functional support (House et al. 1982).

Cross-sectional and prospective analyses document a beneficial effect of the perception of social support and health. Greater levels of perceived social support have been associated with favourable prognoses in coronary heart disease (Berkman 1995) and breast cancer survival rates (Gidron and Ronson 2008) and serve as a protective factor against the increased risk of mortality following stressful life events (Rosengren et al. 1993). In a prospective cohort study of 194 participants, perceived emotional social support was associated with reduced mortality at 6 months following acute myocardial infarction (Berkman et al. 1992) even after controlling for the severity of the MI, comorbidities and socio-demographic variables including socio-economic status. In another longitudinal multi-centre study of 528 haemodialysis and peritoneal dialysis patients, perceiving inadequate levels of social support was associated with mortality at follow-up (mean 911 days) controlling for demographic, socio-economic and biological variables. Evidence suggests that the perception that support exists and can be provided if necessary is equally, if not more effective than the structural components of support.

2.7 **Moderators of social support**

A moderator is a variable that alters the strength or direction of associations between an independent and dependent variable. In the social support literature, gender, ethnicity and psychological factors are implicated as moderators in the association between social support and health.

2.7.v Gender

The receipt, provision and utilisation of social support vary across social groups. Gender variations in social support are most widely reported (Umberson 1992, Eaker et al. 2007). Females report larger and more multifaceted social networks than men. They also provide and receive more support than males. Females are more likely to have a close confidante and their social relations primarily focus on disclosure. Males, on the other hand, are more likely to report their spouse as being their confidante and maintain social networks with a social focus. The smaller network size reported by males renders them emotionally affected by a small number of close individuals, this is in contrast to the pattern observed in females. The gender differences in social support are constant across the adult life course (Shye et al. 1995).

The utility of social support also differs by gender, most evident are the positive effects of marriage in males compared to females (Umberson 1992). Four explanations are proposed for the observed gender differences in social support i) a 'support gap' exists, that is, females give more support to their spouses than they receive (Iida et al. 2010); ii) males want and receive more social support from their spouse, whereas females receive more support from friends and family (Kaplan and Hartwell 1987); iii) females' propensity to very close social relations may become a source of stress rather than support; and iv) females may be more resilient and require less support from their social contacts.

Additionally, gender differences exist in the conditions in which support is provided. Wives may provide increased support when husbands disclose more severe health issues; however the support provided by a husband may not vary according to problem severity (Neff and Karney 2005). Interestingly, these differences are less frequently seen when observing couples in laboratory settings. This either indicates that husbands and wives are equally able to provide spousal support (and that there are simply discrepancies in self-reported support vs observed support), or that a naturally

occurring construct such as social support is unsuitable for study in artificially induced situations. Berkman and colleagues reported that, following the death of a spouse, widowers were at increased risk of mortality but no such increased risk was observed in widows (Berkman et al. 1993).

Although evidence is lacking, females may be more susceptible to the social influence of their networks than males. Health behaviours within a social network may be more transmissible amongst females than males (Smith and Christakis 2008), that is, behaviours more readily spread between social ties. Cross-sectional evidence suggests that friends' dieting is associated with unhealthy weight control behaviours (self-induced vomiting, laxatives, diet pills, or fasting) in average- and over-weight girls (Eisenberg et al. 2005). Similarly, the occurrence of breast cancer in one woman may increase mammography attendance within the social network (Murabito et al. 2001).

Given the variations in the literature, the use of gender as a covariate in analyses may obscure any association between social support and health. Gender stratified analyses are becoming commonplace in social support research (Molloy et al. 2009, Shye et al. 1995). This will be incorporated into the statistical analyses of this thesis.

2.7.vi Ethnicity

Although social support may be a universal resource, ethnic differences in the provision and receipt of social support are reported. However, it is difficult to draw definitive conclusions from the existing evidence base. In certain ethnicities, two social institutions – the family and religious organisations – play a much larger role. Here, strong family ties and relationships with extended family are often more apparent (Stopes-Roe and Cochrane 1990). Stopes-Roe and Cochrane found that South Asians had larger households and received the majority of their support from the 'nuclear

family'. They also had larger networks and reported higher levels of satisfaction with the support they received when contrasted with Europeans. However, there are times where having a very close family network may have a converse effect and result in intergenerational tensions. Results from the Newcastle Heart Project also found that South Asians were more likely to be married or cohabiting than Europeans, have larger households and attended places of worship more frequently (Pollard et al. 2003). The larger emphasis on the importance of family and the size of the family network, notionally increases the presence and likelihood of receiving social support (Vaux 1985). However, South Asian civil servants participating in the Whitehall II study reported lower levels of social support at work and higher levels of negative social support compared to white participants. There was no difference in social support between white and black participants (Hemingway et al. 2001). Furthermore, the Health Survey for England (HSE) found that South Asian and black participants reported less perceived social support than white participants (Shields and Price 2005). There also appear to be ethnic variations in openness to request support, black females being less willing than white females (Ball 1980).

Places of worship are seen as the centre for social and spiritual life. Churches and their congregations, for example, provide social support services to each other and the wider community. By doing so, religious organisations and their congregations form an extended community and social support network for individuals. Established ethnic minority communities may exist in particular geographical areas. This concentration may enhance social cohesion, a sense of community well-being, support and mutual aid (Halpern and Nazroo 2000).

Whilst recognising these resources, social support may be limited for migrants and less established communities. Recent migration is an extremely isolating and stressful experience and establishing oneself in an unfamiliar country and community, new migrants do not have the same supportive environment as indigenous individuals or

settled migrants (Stansfeld et al. 2006). Migration often results in a loss of supportive resources and a sense of heightened stress and alienation.

2.7.vii Depression

Levels of social support vary by depression status. There is consistent longitudinal evidence, in many settings, that low levels of social support are a risk factor for the onset and course of depression. Similarly, depressed individuals are more likely to perceive lower levels of structural and functional support (George et al. 1989), be unmarried and live alone than individuals who are not depressed. The causal direction of this association remains unknown. Three possible explanations are debated: i) inadequate social support leads to the onset of depression, ii) depressed individuals exhaust their supportive resources which results in isolation and iii) depression and its associated symptoms (anhedonia and feelings of hopelessness for example) cause support resources to be viewed through a 'negative lens.' This may mean that depressed individuals do not recognise that support is available and consequently may not utilise the support (Frasure-Smith et al. 2000).

Less is known about whether the association between social support and health outcomes differ according to depression status. Depressed individuals with good levels of social support experience more rapid symptom improvements and less recurrent episodes of depression (George et al. 1989, Henderson et al. 1997). Social support may also serve as a protective modifying factor for physical health in individuals who are depressed. In a prospective study, Frasure-Smith and colleagues (2000) reported that participants with depression who perceived very high levels of social support were at no increased risk of mortality post-acute myocardial infarction at 1 year follow-up. Additionally, depressive symptoms in these individuals were more likely to improve over the study period than those with depression and low levels of social support.

Findings indicate favourable prognoses for depressed individuals with supportive social networks.

2.8 **The direct and buffering effects of social support**

Social support exerts its influence on health in at least two ways: i) social support may have a direct influence on the health of an individual and ii) social support may have an indirect or 'buffering' effect on health (Cohen and Wills 1985).

The direct effect model proposes that social support exerts a direct effect on health independently of whether an individual is under stress (Figure 10). Social support and social networks provide individuals with stable communities or network-based roles and a sense of self-worth. These contacts may provide the support needed to cope with health problems and to adhere to self-care regimens. Support may also help individuals avoid potentially negative and damaging situations, such as economic problems, that may otherwise impact upon mental and physical health. Additionally, social support may have direct physiological effects on cardiovascular, neuroendocrine or immune system functioning. Social support is associated with reduced cardiovascular reactivity in times of stress, lower cortisol levels and lower levels of C-reactive protein and other inflammatory markers (Uchino 2006).

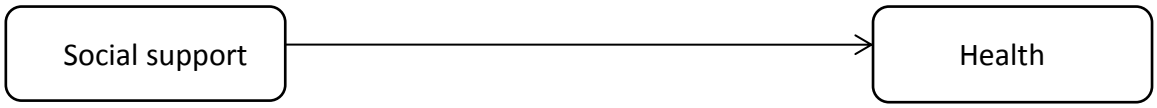


Figure 10 The direct effects model

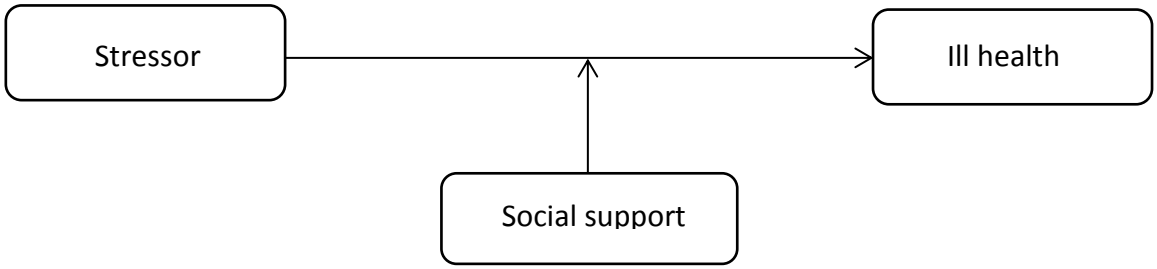


Figure 11 The buffering effects model

The indirect, or buffering, model proposes that social support primarily influences the health of individuals under stress (Cohen and Wills 1985) (Figure 11). In this model, social support 'buffers' (protects) individuals from the potentially adverse impact of stressful events. This can happen in two ways, psychologically or physiologically. Firstly, social support may intervene between a stressful event and a stress reaction by preventing a stress appraisal response. The perception that others will provide the necessary support may lead to a reappraisal of the potentially stressful event. This increases one's perceived ability to cope with the threat and subsequently diminishes its perception as highly stressful. Secondly, sufficient social support may influence physiological processes between a stressful event and stress reaction by reducing or eliminating the stress response (Cohen and Syme 1985).

2.9 **Social support and type 2 diabetes**

For the most part, social support is beneficial in the management of both acute and chronic conditions. In diabetes, social support appears to be associated with improved diabetes self-management; following a healthy eating plan, increasing physical activity,

performing foot checks and adhering to blood glucose monitoring and to medication regimens (Tang et al. 2008, Garay-Sevilla et al. 1995, Sherbourne et al. 1992, Pham et al. 1996, Schiotz et al. 2012). However, the association between social support and glycaemic control in type 2 diabetes is inconclusive (Mani et al. 2011, Connell et al. 1992). Before the mechanistic routes of action can be investigated and interventions developed, it is important to determine whether an association exists in the first instance. We conducted a systematic review of published and unpublished observational studies investigating the association between social support and glycaemic control in adults with type 2 diabetes (Chapter 3).

2.10 **Summary**

In social epidemiology, the concept of social support has been a focus of study for over 25 years. It is now accepted that social support is an independent predictor of biomedical outcomes, morbidity and mortality across a range of conditions. Social support may either have direct effects on health outcomes (independently of whether the individual is under stress) or buffer the potentially damaging effects of stressful events which consequently lead to ill health, but methodological concerns about the definition and measurement of social support are currently hampering the progression of the literature in this area. The majority of research has taken place in cardiovascular disease, where social support appears to be protective against recurrent events and mortality but the evidence base in type 2 diabetes is lacking and inconsistent. The next chapter is a systematic review of observational studies examining the association between social support and glycaemic control in type 2 diabetes.

Chapter 3 Social support and glycaemic control in type 2 diabetes

3.1 **Synopsis**

This chapter is our systematic review entitled: Social support and glycemic control in type 2 diabetes: A systematic review of observational studies, which has been published in the journal Patient Education and Counseling (Stopford et al. 2013)(Appendix I)[1].

To date, there has been no systematic review of the association between informal social support (support from family and friends as opposed to health care professionals) and glycaemic control in type 2 diabetes. We searched MEDLINE, PsycINFO, EMBASE, Scopus, Web of Science and Sociological Abstracts to July 2012 for observational studies investigating the association between structural or functional aspects of social support (social networks, community ties, marital status, family support, perceived, actual, emotional or instrumental social support) and glycemic control (HbA1c). From electronic and reference searches, 29 studies were eligible. Twenty different assessments of social support were used. Family support and composite measures of support were most frequently associated with reduced HbA1c. There was no evidence for a beneficial effect of other support measures on HbA1c. We found marked variation in population, setting, measurement of social support and definition of outcome, limiting the methodological validity of research. Social support may be important in the management of type 2 diabetes, the need for consensus and standardization of measures is highlighted.

[1] As this paper was published in an American journal the contents of this chapter use American English.

3.2 **Introduction**

Social support is an important explanatory variable with prognostic significance for health outcomes (Marmot 2005, Cohen 2004, Uchino 2006). The self-management of type 2 diabetes mellitus is cornerstone to achieving good glycemic control and reducing the risk of developing microvascular (retinopathy, nephropathy and neuropathy) and macrovascular (cardiovascular and cerebrovascular disease) complications. The management of diabetes necessitates an active role of the patient. This involves lifestyle modifications such as improving diet, increasing physical activity, self monitoring of health status (blood glucose and examination of feet), acquisition of diabetes knowledge as well as adherence to professional advice.

Recently, there has been an increase in research into the supportive role of healthcare professionals, diabetes education and patient participation groups in the management of type 2 diabetes ; support that can be classified as 'formal'. The role of more informal interpersonal relations in diabetes care, that is, the presence or support provided by social networks or family members has been less studied. Social support comprises of structural and functional elements (Lin et al. 1999). These elements vary in their characteristics and in their effects on health (Uchino 2009, Holt-Lunstad et al. 2010). The structural aspects of support refer to webs of social relationships and linkages which are best measured through quantitative scoring of the size of networks or existence of support resources (marital status, social networks and community ties). Functional components (social support) are elicited from the structural basis of social relations (Lin et al. 1999). The existence and quantity of social relationships do not necessarily provide social support, however they certainly increase the likelihood of receiving help when needed. Social support functions are more consistently associated with health outcomes than structural aspects of support (Uchino 2009). However, not all support is helpful. The term 'social support' carries positive connotations. Social support may often be wanted, but can result in misconstrued social pressure, such as nagging or criticism, or unwanted (negative) outcomes (Clark and Nothwehr 1997).

In health, social support is purported to exert its influence in two main ways: 1) directly: providing necessary support to cope with health problems, adhere to self care regimen and avoid potentially negative situations (for example, economic problems) or 2) indirectly: acting as a buffer (protection) against the impact of stressful events (Cohen and Wills 1985).

In diabetes, both mechanistic routes of action may lead to improved glycemic control. Social support is associated with increased adherence to diabetes self care (Tang et al. 2008, Garay-Sevilla et al. 1995, Sherbourne et al. 1992, Pham et al. 1996, van Dam et al. 2005, Gallant 2003, Schiotz et al. 2012), however there is a lack of consensus as to whether this translates into improved biomedical outcomes. A recent meta-analysis of six randomized controlled trials (RCT) of formal supportive interventions (group visits to clinician, telephone and internet support, spouse involvement and family and friend support in interventions) for patients with type 2 diabetes (pooled n=712) tentatively reported favorable results in diabetes self-management and biomedical outcomes (van Dam et al. 2005). Biomedical outcomes were assessed in four of the trials and improved in two, although effects were seen in different bio-markers. HbA1c and lipids improved following group visits to the clinician (Trento et al. 2001) and BMI improved following spouse involvement in diabetes weight-management education in women only (Wing et al. 1991). Across trials, improvements were also seen in diabetes self care, quality of life and diabetes knowledge (Wing et al. 1991, Trento et al. 2001, Keyserling et al. 2002, Gilden et al. 1992).

There is some evidence to suggest that formal social support is effective in improving glycemic control. However, RCTs artificially introduce social support. There is rich data available from observational studies which may allude to the, as yet unidentified, active ingredients of support. By using observational data to understand the active ingredient this can then be translated into RCTs. Furthermore with increasing pressure on healthcare systems, formalized support interventions are expensive to provide, rigid and risk not engaging some individuals. On the other hand, informal support, such

as that provided by significant others, friends and family, is 'free', readily available and specific to the individual. Investigating these constructs in the context of long term conditions such as type 2 diabetes may be important in the support of self-management. Evidence from observational studies is the main method by which to study such associations.

The social determinants of biomedical outcomes in type 2 diabetes is an understudied area. Due to the epidemic of type 2 diabetes and its increasing societal and economic burden, the need to identify non pharmacological, cheap and modifiable targets for intervention is increasing. Our aim is to systematically review published and unpublished literature investigating the association between informal social support and glycemic control in adults with type 2 diabetes.

3.3 **Methods**

Eligible studies were those meeting the following inclusion criteria: observational studies (case control, cohort and cross-sectional studies) of adults (≥ 18 years of age) with type 2 diabetes or non insulin dependent diabetes, that investigated the relationship between social support and glycemic control; studies with a primary or secondary emphasis on the association between social support and glycemic control were eligible; studies utilizing measures assessing structural and functional components of (informal) social support: marital status, family support, social networks, and community ties (involvement in social structures within the community), perceived, actual, instrumental (tangible assistance) or emotional social support. Terms were chosen to cover a wide range of support measures from a socio-ecological perspective. Studies measuring other types of social support were excluded. Any variables focusing solely on formal professional support, support from healthcare providers and support from diabetes education programs were also excluded. Studies combining type 1 and type 2 diabetes were excluded unless data for type 2 diabetes

were reported or could be obtained from respective authors. Studies that were purely descriptive in nature without the use of statistical analysis were excluded as these studies provide no data to quantify associations between social support and glycemic control.

Our main outcome measure was long term glycemic control based on the percentage of glycated hemoglobin (HbA1c). In type 2 diabetes the National Institute for Health and Care Excellence (NICE) states that the target HbA1c should be between 6.5% and 7.5% (42 mmol/mol and 58 mmol/mol) based on individual risk for micro- and macro-vascular complications (McIntosh et al. 2001).

The search strategy included several data sources. Electronic database searches were carried out on the following databases: Medline (1946 – 2012), Embase (1947 – 2012), PsycInfo (1806 – 2012), Scopus (1960 – 2012), Web of Science (1899 – 2012) and Sociological Abstracts (1952 – 2012). Searches were run on the 11th July 2012. The search was restricted to studies of human beings but was not restricted by language or publication year. Any duplicate results were combined.

To capture the broadest sample of relevant studies we used multiple search terms. The following search terms were used for MEDLINE and adapted for the other databases: exp Diabetes Mellitus, Type 2 and exp social support or (social adj support).mp or exp Marital Status or (marital adj status).mp or exp Spouses or (social adj network).mp. or exp Family and HbA1*.mp. or glyc?emic control.mp or A1c.mp. or GHb.mp. or Glycoh?emoglobin.mp. or Glyc* h?emoglobin.mp. and exp Epidemiologic Studies/ or exp Case-Control Studies/ or exp Cohort Studies/ or case control.tw. or (cohort adj (study or studies)).tw. or Cohort analy*.tw. or (follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or longitudinal.tw. or retrospective.tw. or cross sectional.tw. or Cross-Sectional Studies/.

The reference lists of eligible studies were hand searched for additional studies not identified by the search. Related reviews retrieved in the search were also checked for relevant citations. The conference proceedings of the American Diabetes Association, Diabetes UK and the European Association for the Study of Diabetes from July 2009 to July 2012 were searched under social, psychological and behavioral sub headings. Leading authors in the field were contacted for additional data on published or unpublished studies.

The abstracts and titles of studies identified by the search strategy were screened for potentially relevant studies by one author (RS). Manuscripts included based on their abstract were obtained as full text documents which were screened for potential inclusion in the review. In the case of ambiguity, the full text was retrieved. Any discrepancies were discussed and resolved through consensus with the co-authors (KW AND KI).

For selected studies, we coded in a standardized manner the following characteristics (when available) of the study sample: country, number of participants, type of study, setting and sampling method, age, gender, duration of diabetes, social support measure, outcome measure, confounding variables and the main findings. An attempt was made to retrieve missing or incomplete data from studies by fax or e-mail. Odds ratios (OR) or standardized beta values were reported when possible. Otherwise, other measures of associations or values of statistical significance of the reported association were given. Studies often investigated a number of explanatory variables and dependent variables. Only associations including social support measures are reported.

There is a lack of consensus regarding the optimal method of assessing quality in observational studies (Sanderson et al. 2007). All eligible studies were included and

quality was assessed. Quality was defined as the confidence that the design, conduct and analysis of each study minimized bias in the estimation of the effect of the exposure on the outcome. Quality assessment was based on checklist items from the PRISMA statement (Moher et al. 2009). We assessed i) description of participant characteristics, ii) quality of study design, iii) method of recruitment, iv) validity of measures, v) validity of outcome measurement and vi) controlled for confounding variables. The quality of studies was not summarized using scores. Summary scores are often problematic as weighting of component items and domains are often variable and inconsistent across scales (Jüni et al. 2001). Studies were considered to be of good quality if they used a prospective design, consecutive or random sampling of study participants, utilized validated instruments for exposures, defined the outcome and controlled for confounding variables.

3.4 **Results**

The search strategy yielded 874 studies. Reference searching, conference proceedings and expert advice identified a further 17 studies and 90 studies were selected for full text review (Figure 12). Data extraction from the full texts identified 23 studies from the electronic database search, 4 manuscripts from the reference search and 2 abstracts from conference proceedings for inclusion. Reasons for exclusion from the review are shown in Figure 12.

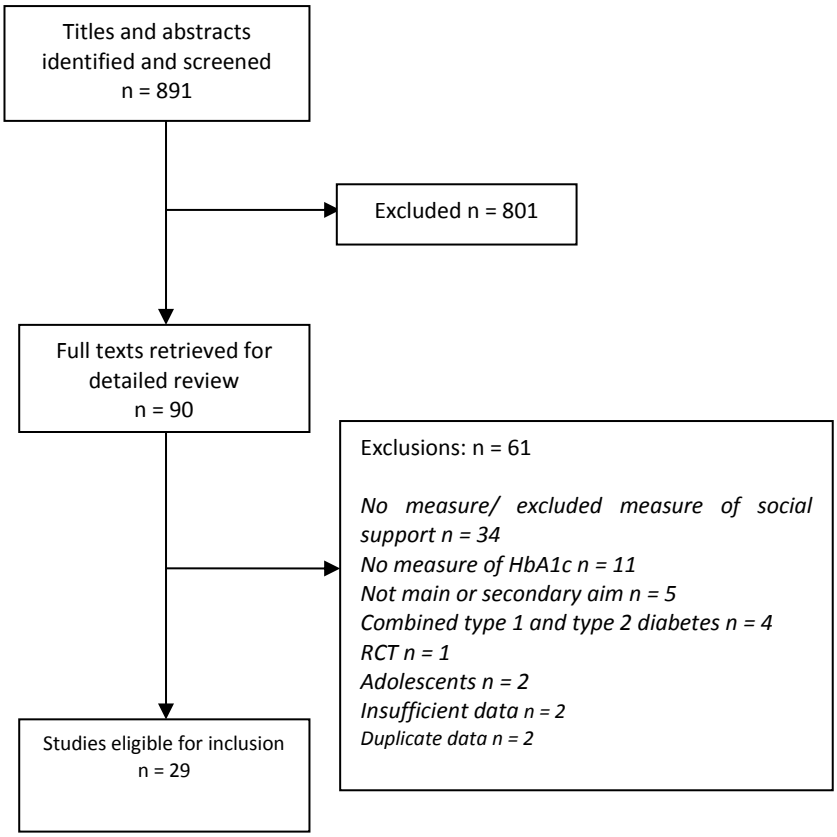


Figure 12 Flow chart of the systematic review

The studies included in the systematic review are listed in Table 3. Sixteen of the 29 studies were conducted in the United States and 4 were conducted in European countries, but not in the UK. Of the 29 studies included, the designs were: 25 cross-sectional, 3 cohort and 1 case control. The mean age of study populations ranged from 50.6 years to 69.2 years in the 26 studies that reported age, all but one study included both male and female populations. Three studies did not report gender. Sample sizes ranged from 53 to 2572 participants. The independent variable (social support) was assessed by self-report in all included studies. Measures of social support were varied, with little overlap across studies. The most frequently used measures were multidimensional assessments of social support (measures that assessed more than one component of social support) (n = 16) (Huang et al. 2010, Chew et al. 2011, Fortmann et al. 2011, Howteerakul et al. 2007, Misra and Lager 2009, Nozaki et al. 2009, Okura et al. 2009, Wilson et al. 1986, Whittemore et al. 2005, Osborn et al. 2010, Nakahara et al. 2006, Schillinger et al. 2002, Sukkarieh-Haraty et al. 2012, Kacerovsky-

Bielesz et al. 2009, Kaplan and Hartwell 1987, Chlebowy and Garvin 2006). Of these, 13 studies generated a composite measure of social support and 3 studies separated analysis by social support type (Chlebowy and Garvin 2006, Kaplan and Hartwell 1987, Kacerovsky-Bielesz et al. 2009). Seven studies investigated family support measures (Choi and Rankin 2009, DuVal et al. 2011, Ilias et al. 2001, Thaneerat et al. 2009, Mayberry and Osborn 2012, Dai 1996, Venkataraman et al. 2012), 10 assessed marital status (Blaum et al. 1997, Schiotz et al. 2012, Souza et al. 2011, Thaneerat et al. 2009, Peyrot et al. 1999, Dai 1996, Venkataraman et al. 2012, Kirk et al. 2011, Rahman et al. 2008, Pons 2011), 5 studies assessed network size (Chlebowy and Garvin 2006, Ilias et al. 2001, Schiotz et al. 2012, Kaplan and Hartwell 1987, Rothenbacher et al. 2003) and 1 assessed perceived social support (Kim 2011). There were no studies that utilized measures of community ties or that assessed stand-alone measures of actual, instrumental or emotional support although the latter were included in the measure used by Kacerovsky-Bielesz et al. (2009). Five studies used more than one measure to assess social support (Dai 1996, Ilias et al. 2001, Schiotz et al. 2012, Thaneerat et al. 2009, Venkataraman et al. 2012). Eight studies assessed support specific to diabetes care (Choi and Rankin 2009, Howteerakul et al. 2007, Mayberry and Osborn 2012, Okura et al. 2009, Schillinger et al. 2002, Sukkarieh-Haraty et al. 2012, Whittemore et al. 2005, Venkataraman et al. 2012) and two studies used measures of social support specific to chronic disease (Fortmann et al. 2011, Nozaki et al. 2009). We did not separate results into functional and structural support due to heterogeneity in measurements of social support.

3.4.i Exposure measurements

Marital status: Ten studies investigated the association between marital status and glycemic control. Two studies report being married (Rahman et al. 2008) and living with a partner (Schiotz et al. 2012) to be independently associated with increased HbA1c. Eight studies reported no association between marital status and HbA1c

(Blaum et al. 1997, Kirk et al. 2011, Souza et al. 2011, Thaneerat et al. 2009, Peyrot et al. 1999, Dai 1996, Venkataraman et al. 2012, Pons 2011).

Social networks: Four studies assessed the association between social network size and HbA1c. Kaplan and colleagues found no relationship between social network size and HbA1c at baseline but at 18 months large social network size was found to be associated with a reduction in HbA1c in men (Kaplan and Hartwell 1987). Conversely, Rothenbacher and colleagues found large social networks to be associated with increased HbA1c (Rothenbacher et al. 2003). Two studies reported no significant association between social network size and HbA1c (Chlebowy and Garvin 2006, Schiotz et al. 2012). Kaplan and Hartwell and Chlebowy and Garvin utilized the Social Support Questionnaire which additionally measures satisfaction with network support. In a prospective study of a RCT cohort, support was significantly associated with lower HbA1c in males but increased HbA1c in females. No association was seen in change in HbA1c at 18 months follow-up (Kaplan and Hartwell 1987). In their cross-sectional study, Chlebowy and Garvin (2006) report no significant association between satisfaction with network support and HbA1c.

Family support: Choi and colleagues assessed family support using the Diabetes Family Behavior Checklist-II (DFBC-II). The DFBC diet subscale, but not the exercise subscale, was independently associated with lower HbA1c (Choi and Rankin 2009). A smaller study by Mayberry and colleagues did not find this association (Mayberry and Osborn 2012). Perceived family support assessed using the Family Support Scale (FSS) was associated with lower HbA1c levels (Ilias et al. 2001). Gender differences were reported in a study of 152 patients in Taiwan (Dai 1996). Family support (FSS) was independently associated with higher HbA1c in females and lower HbA1c in males. Three studies reported no significant association between family support and HbA1c (DuVal et al. 2011, Thaneerat et al. 2009, Venkataraman et al. 2012).

Perceived social support: Kim and colleagues found perceived spousal support to be independently associated with reduced HbA1c in male, but not female, patients (Kim 2011).

Multifaceted measurements: Five (out of 13) studies found social support to be independently associated with HbA1c. Okura and colleagues found low and intermediate support (assessed using the subsection of the Diabetes Care Profile (DCP)) to be independently associated with higher HbA1c (Okura et al. 2009). Similarly, Whittemore and colleagues found increased social support (measured using the support subscale of the DSMART) to be independently associated with lower HbA1c in a female sample (Whittemore et al. 2005). Kacerovsky-Bielesz and colleagues assessed four dimensions of social support using the Berlin Support Scales (Kacerovsky-Bielesz et al. 2009). Increased emotional support was independently associated with increased HbA1c in men only. No association with HbA1c was seen on other dimensions of social support (instrumental, informational or satisfaction). In unadjusted analysis, Misra and Lager report greater social support (assessed using the Personal Resource Questionnaire – II), to be associated with lower HbA1c (Misra and Lager 2009). Similarly, Fortmann and colleagues utilized 13 items from the Chronic Illness Resource Survey (Chandola and Jenkinson) to assess support received over the previous three months (Fortmann et al. 2011). In unadjusted analysis, increased social support was associated with lower HbA1c. Self-management and depression mediated this relationship. Sukkarieh-Haraty reports a significant association in the opposite direction. Social support (measured using the DCP) is independently associated with increased HbA1c (Sukkarieh-Haraty et al. 2012).

No associations were observed in 9 studies when measuring social support using the following measures: Social Support Scale for Patients with chronic disease (Nozaki et al. 2009), adapted questions from the Diabetes Care Profile (Schillinger et al. 2002), The Social Support Survey (Chew et al. 2011) the Social Support Scale modified from

the Michigan Diabetes Care Profile (Howteerakul et al. 2007) or The Interpersonal Support Evaluation List (ISEL) (Wilson et al. 1986).

3.4.ii Outcome measurement

Glycemic control: The measure of glycemic control was HbA1c in all studies. Sixteen studies collected venous or capillary blood samples to assess HbA1c. Eight studies recorded HbA1c from medical records (Kirk et al. 2011, Mayberry and Osborn 2012, Misra and Lager 2009, Nozaki et al. 2009, Peyrot et al. 1999, Schillinger et al. 2002, Souza et al. 2011, Dai 1996). Two studies used self reported HbA1c (Kim 2011, Schiotz et al. 2012), 1 study obtained HbA1c values from home test kits (Okura et al. 2009), and 1 study used the mean value of the 3 most recent HbA1c results over 3 years (Chew et al. 2011). One study reported no information as to how HbA1c was obtained (Rothenbacher et al. 2003). Ten studies measured HbA1c categorically. The definition of poor glycemic control varied between studies ranging from >6.5% (42 mmol/mol) (Misra and Lager 2009) to ≥11.6% (102 mmol/mol) (Blaum et al. 1997). The remainder of studies (n = 19) examined HbA1c as a continuous variable.

3.4.iii Quality Assessment

All but one study (Pons 2011) adequately described participant characteristics . Two studies included in this systematic review used a prospective design (Kaplan and Hartwell 1987, Nozaki et al. 2009) with a mean follow-up period of 15 months. Two of the included studies used random sampling methods (Rahman et al. 2008, Blaum et al. 1997) and 5 used consecutive sampling (Kacerovsky-Bielesz et al. 2009, Rothenbacher et al. 2003, Schillinger et al. 2002, Whittemore et al. 2005, Kirk et al. 2011). Of the 23 studies using questionnaires to assess levels of social support, 9 studies (DuVal et al. 2011, Okura et al. 2009, Rothenbacher et al. 2003, Schillinger et al. 2002, Sukkarieh-

Haraty et al. 2012, Thaneerat et al. 2009, Venkataraman et al. 2012, Kim 2011, Ilias et al. 2001) (including 2 conference abstracts) did not report any information about the reliability or the validity of the social support measures. The remainder of studies assessed marital status only (n = 6). One study did not report how HbA1c was measured (Rothenbacher et al. 2003). Sixteen studies controlled for confounding variables when assessing the association between social support and glycemic control. In 5 additional studies, adjusted analysis was conducted, but social support was not entered due to insignificant associations between social support and glycemic control in unadjusted analysis (Blaum et al. 1997, DuVal et al. 2011, Thaneerat et al. 2009, Venkataraman et al. 2012, Howteerakul et al. 2007). There were no studies included in this review that assessed all 6 quality criteria, 4 studies met 5 out of 6 quality criteria (Kaplan and Hartwell 1987, Rahman et al. 2008, Kacerovsky-Bielesz et al. 2009, Kirk et al. 2011).

Table 3 Summary of studies included in the systematic review

First author, year, country.	*Setting, sampling method*	*Sample Size (% women)*	*Age, mean (SD/range)*	*Average duration of diabetes years (SD/range)*	*Measure of social support*[a]	*Adjusted for confounders*	*Measure of glycemic control*[b] *(%)*	*Main findings*[c]
Cross sectional study design								
Mayberry, 2012, USA	Primary care, convenience	61 (69)	57.1 (8.6)	8.0 (6.1)	Adapted version of the Diabetes Family Behavior Checklist (DFBC): family support in diabetes	None	HbA1c	Unadjusted: no association between DFBC and HbA1c^ Note: perceiving family members as non supportive was associated with poor medication adherence (r = 0.44p < 0.001) which was associated with HbA1c (r = 0.24p = 0.03)
Schiotz, 2012, Denmark	Primary care, convenience	2572 (34)	60.5 (10.5)	10.0 (8.0)	Questions from Danish population health-profile studies: 1) Social network structure: living with partner/contact with family and friends 2) Social network function: confidence in support in the case of severe illness	PACIC	Categorical HbA1c (≤7 = good control / >7 = poor control)	Unadjusted**: 1) Living with a partner was associated with higher HbA1c (p = 0.002). Meeting with family (p = 0.9) or friends (p = 0.64) > once a month was not associated with HbA1c 2) Social network function was not associated with HbA1c (p = 0.08)
Sukkarieh-Haraty, 2012, Lebanon	Outpatient, convenience	140 (57.1)	18-29=1.4% 30-39=2.1% 40-49=10% 50-59=37.1% 60-69=25% >70=22.9%	0-5yrs=34.3% 5-10yrs=27.1% 11-16yrs=17.9% ≥17yrs=20.7%	Diabetes Care Profile: Social support scale.	Age, sex, treatment, diabetes associated problems, BMI	HbA1c	Social support was significantly associated with increased HbA1c (beta = 0.02, p = 0.01).
Chew, 2011, Malaysia	Primary care, convenience	175 (66.3)	62.7 (10.8)	11.7 (6.7)	1) The Medical Outcomes Study Social Support Survey:- Structural support: 2) number of supporters Functional support: 3) emotional/informational support 4) tangible support 5) positive social interaction 6) affectionate support	None	HbA1c	Unadjusted: no association between social support and HbA1c. 1) social support score (r = -0.06, p = 0.47) 2) number of supporters (r = -0.03, p = 0.68) 3) emotional/informational support (r = -0.06, p = 0.46) 4) tangible support (r = 0.03, p = 0.74) 5) positive social interaction (r = -0.04, p = 0.59) 6) affectionate support (r = 0.04, p = 0.62)
Fortmann, 2011, USA	Community, convenience	208 (71)	50.6 (10.9)	NR	Chronic Illness Resource Survey (Chandola and Jenkinson): support received over 3 months from friends, family, healthcare providers, community and personal support	None	HbA1c	Unadjusted: association between CRIS and HbA1c (r = -0.16, p < 0.05). Notes: relationship between CRIS and HbA1c was mediated by diabetes self management and depression

Kirk, 2011, USA	Primary care, consecutive	669 / 1398 (60.5)	59.8 (12.9)	NR	Marital status	Sex, ethnicity, BMI, tobacco use, LS, insurance, education, income, exercise, diabetes education	Categorical HbA1c (≤7 = good control)	Marital status did not predict HbA1c^
Venkataraman, 2011, India	Tertiary care, convenience	507 (55)	54 (Census 2011)	6.5 (5.9)	1) Family support for diabetes self care 2) Marital status	None	HbA1c	Unadjusted: no association between family support or marital status and HbA1c^
Kim, 2010, USA	NR, NR	68	NR	NR	Perceived spouse support	Sex- others NR	HbA1c	Perceived spouse support was associated with HbA1c in males but not females*
Pons, 2010, USA	NR, NR	698/ 1427	NR	NR	Marital status	NR	Categorical HbA1c (≤7/>7)	Marital status was not a predictor HbA1c < 7%^
Souza, 2010, Brazil	Primary care, convenience	146 (71.7)	61.1 (11.2)	1-5yrs=54.4% 6-10yrs=29.9% 11-15yrs=13.4% ≥16 yrs=6.3%	Marital status	Socio-demographic, disease-specific, clinical and psychological measures	HbA1c	Marital status was not a significant predictor of HbA1c (beta = -0.08, p = 0.03)
Choi, 2009, USA	Community, convenience	143 (51.7)	62.4 (12.8)	6.8 (6.2)	Diabetes Family Behavior Checklist-II (DFBCII): 1) Diet subscale: positive and negative family support specific to diet 2) Exercise subscale: positive and negative family support specific to exercise.	Age, sex, education, acculturation, BMI, WHR, DD, diabetic medications	HbA1c	1) DFBC-II diet subscale predicted HbA1c (β = -0.170, p = 0.03) 2) DFBC-II exercise subscale not entered (not significantly associated with HbA1c in unadjusted analysis (r = -0.14, p > 0.05))
Kacerovsky-Bielesz, 2009, Austria	Outpatient, consecutive	257 (50.97)	64 (9)	14 (9)	Berlin Social Support Scales (BSSS): 1) emotional 2) instrumental 3) informational 4) support satisfaction	Socio-demographic, disease-specific, clinical and anthropometric and psychological measures	HbA1c	1) Emotional support was associated with HbA1c in males (beta = 0.516, p = 0.007). No association in females^. 2) instrumental support not associated with HbA1c in men (beta = -0.33, p = 0.07) or women^ 3) informational support was not associated with HbA1c in men^ or women^ 4) support satisfaction was not associated with HbA1c in men (beta = -0.31, p = 0.054) or women^
Okura, 2009, USA	Community, convenience.	1097 (51.9)	69.2	≤10yrs=56.4% 11-20yrs=24.7% ≥ 21yrs=18.9%	Social support subsection of the Diabetes Care Profile: how much patients could count on family or	Age, sex, ethnicity, cognitive function education, income, insurance status,	Categorical HbA1c (< 7.0 7.0 – 7.9	Intermediate and low social support was associated with higher HbA1c than those with high social support (OR = 1.50, 95% CI 0.82-

					friends to help with diabetes care	DD, depression, understanding of diabetes, hyperglycemic treatment, functional limitations, comorbidity	≥ 8.0)	2.74 and OR = 1.41, 95% CI 0.83-2.41 respectively)
Thaneerat, 2009, Thailand	Outpatient, systematic	250 (64.4)	62.6(10.41)	12.8 (8.35)	1) Marital status 2) Questionnaire for Assessment of Social Support: family support	None	Categorical HbA1c (≤7 = good control)	Unadjusted: no association between marital status or social support and HbA1c^
Rahman, 2008, Malaysia	Primary care, stratified random	219 (59.6)	55.6 (8.55)	6 (IQR =7)	Marital status	Occupation, educational level, smoking, FH, health centre with family medicine specialist, FBG, Cholesterol, Triglycerides, HDL-cholesterol, LDL cholesterol, BMI, sBP, dBP	HbA1c	Being married was associated with increased HbA1c (beta = 0.93, 95% CI= 0.43, 1.44)
Howteerakul, 2007, Thailand	Tertiary care, convenience	243 (65.8)	60.2 (37-79)	Median = 7 (range= 1-40 yrs)	Social support scale modified from the Michigan Diabetes Care Profile: support from family and friends	None	Categorical HbA1c (≤7 = good control)	Unadjusted: high social support did not display significantly better HbA1c than those with low social support (OR 1.32, 95% CI 0.74, 2.36)
Misra, 2007, USA	Primary care, convenience	180 (52)	54.8	NR	Personal Resource Questionnaire – Part II (PRQ8): perceived social support and adequacy of support	None	Categorical HbA1c (≤6.5 = good control)	Unadjusted: more social support was associated with better HbA1c (p = 0.04)
Chlebowy, 2006, USA	Outpatient, convenience	91 (56)	54.96 (12.5)	7.1 (6.5)	Social Support Questionnaire:- 1) Number of supportive individuals (SSQ N) 2) Satisfaction with support (SSQ S)	None	HbA1c	Unadjusted: 1) SSQ N and HbA1c: no association^ 2) SSQ S and HbA1c: no association^
Whittlemore, 2005, USA	Outpatient, consecutive	53 (100)	57.6 (10.9)	2.7 (3.0)	Diabetes self-management assessment tool (DSMART) subscale: confidence in diabetes self management, family / friend and professional support	BMI	HbA1c	Support was a significant predictor of HbA1c (beta = -0.41, p = 0.01)
Schillinger, 2002, USA	Primary care, consecutive	408 (58)	58.1 (11.4)	9.5 (8.0)	Adapted version of the Diabetes Care Profile: family and friend support with diabetes management	Age, sex, education, insurance, language, diabetes education, depression, treatment, DD, clustering within physicians, health literacy	HbA1c	Social support was not a predictor of HbA1c (beta = 0.0002, p = 0.99).

Ilias, 2001, Greece	Outpatient, convenience	98 (26.5)	57.1 (15.3)	10.4 (6.9)	1) Family Support Scale (FSS): perceived family support 2) The number of family members	None	HbA1c	Unadjusted: 1) Association between FSS and HbA1c (r = -0.41, p = 0.05) 2) No association between the number of family members and HbA1c (r = 0.10, p > 0.05).
Blaum, 1999, USA.	Primary care, random	393 (54)	63 (Census 2011)	8.9 (7.8)	Marital status	None	Categorical (HbA1c ≥11.6 = poor control)	Unadjusted: no association between marital status and HbA1c^
Peyrot, 1999, USA	Outpatient, convenience	61 (50.5)	53.3 (0.7)	8.2 (7.0)	Marital status	Sex, education, DD, BMI.	HbA1c	Marital status was not a predictor of HbA1c (beta = 0.02, p > 0.05)
Dai, 1996, Taiwan	Outpatient, convenience	150 (56.7)	63.7 (7.4)	10.6 (6.7)	1) Marital status 2) Family support scale (FSS): adapted from the Personal Resources Questionnaire–85 Part II: emotional support, informational exchange, affirmation and reciprocity. Additional items measured tangible aids and recuperating atmosphere of the family.	Age, sex, education, finance, living arrangements, BMI, DD, hypertension, expectation of filial piety, recent life stress	HbA1c	1) marital status was not a predictor of HbA1c (beta = 0.07, p > 0.05) 2) FSS was not a predictor of HbA1c (beta = 0.06, p > 0.05) Gender differences: increased FSS was associated with higher HbA1c in females (beta = 0.21, p < 0.05) but lower HbA1c in males (beta = -0.23, p = <0.05)
Wilson, 1986, USA	Community, convenience	184 (66.8)	57.9 (10.2)	8.0 (7.5)	The Interpersonal Support Evaluation List (ISEL): perceived social support: appraisal, belonging, tangible, self esteem	Age, sex, health beliefs, stress, knowledge, anxiety, depression	HbA1c	Social support was not a significant predictor of HbA1c (p > 0.05)^
Case control study design								
Du Val, 2011, USA	Outpatient, NR.	246	NR	NR	Support sources in themselves or their family	None	Categorical HbA1c (≥9=cases/ ≤7=controls)	Unadjusted: no association between social support and HbA1c (p = 0.85)
Cohort study design								
Nozaki, 2009, Japan	Outpatient, convenience	304 (44.07) Year 1:	61.9 (Census 2011)	NR	Social Support Scale for patients with chronic disease: emotional support and behavioral support	None	HbA1c	Unadjusted: baseline: no association between the Social Support Scale and HbA1c (r = -0.05, p = 0.37) Year 1: no association between Social Support Scale and HbA1c (r = -0.05, p = 0.36)
Rothenbacher, 2002, Germany	Primary care, consecutive	845 (52.6)	67.3 (40-91)	0-5yrs=38.7%, 5-10yrs=32.5%, >10 yrs=28.8%	Social support: number of people patients can talk to about personal problems	Age, sex, education, MS, occupational status, smoking status, alcohol consumption,	Categorical HbA1c (≥8 = poor	Unadjusted: more individuals in the low social support categories had an HbA1c ≥ 8% (p = 0.02)

						PA, BMI, DD, diabetic medication, compliance, health status	glycaemic control)	Adjusted: social support was not a predictor of HbA1c ≥ 8%^
Kaplan, 1987, USA	Community, convenience	37 (54)	52.97 (13.0)	NR	The Social Support Questionnaire (SSQ): 1) number of support persons in network (SSQ-N) 2) satisfaction with support (SSQ-S)	Sex	HbA1c	1) No association between SSQ-N and HbA1c at baseline. At 18 months: SSQ-N was associated with change in HbA1c in males ($r = -0.3$, $p < 0.05$) but not in females ($r = 0.19$, $p > 0.05$) 2) association between SSQ-S and HbA1c in males ($r=0.36$, $p<0.05$) and females ($r=-0.32$, $p<0.05$) At 18 months: SSQ-S was not associated with change in HbA1c^

FBG: fasting blood glucose; BMI: body mass index; MS: marital status; LS: living status; DD: duration of diabetes; PA: physical activity; PAID: problem areas in diabetes; SES: socioeconomic status; FH: family history of diabetes; HDL: high density lipoprotein; LDL: low density lipoprotein; sBP: systolic blood pressure; dBP: diastolic blood pressure; PACIC: Patient Assessment of Chronic Illness Care; NR: not reported.

a Numbering before variables denote analyses were conducted separately for variables, order of social support measure matches order of findings.
b HbA1c measured as a continuous variable unless specified otherwise.
c Results are adjusted unless specified otherwise.
d No data available. Gray literature abstract. Full text could not be obtained.
e Only unadjusted statistics reported. No significant change when adjusting for PACIC scale.
f No statistics available.

3.5 **Discussion**

We conducted a systematic review of published and unpublished observational studies examining the relationship between social support and HbA1c in adults with type 2 diabetes. There is some evidence for a beneficial effect of social support (family support and multi-dimensional assessments of social support) on glycemic control. There was limited evidence that being married or living with a partner was associated with worse glycemic control. The majority of statistical associations in the review were not significant.

In keeping with the social support literature, this review noted gender differences in the association between social support and glycemic control. However, there was a lack of consensus across studies regarding the direction of this relationship. In prospective analysis, men with larger social networks displayed a greater reduction in HbA1c than women (Kaplan and Hartwell 1987), similarly, in cross sectional analysis, family support was associated with reduced HbA1c in males, but increased HbA1c in females (Dai 1996). The lack of gender specific analyses may have obscured any effect of social support on glycemic control. Informal support seeking is often different in males and females. Females seek and receive more support from friends and extended family, males often seek and receive more support from their spouse (Kaplan and Hartwell 1987). Females may also be more susceptible to the stresses of their social relations. The association between being married and poor glycemic control in two studies was surprising due to a consistently reported protective effect of marriage (Cohen 2004, Berkman et al. 2000), particularly in males (Umberson 1992). Failure to acknowledge these sex differences may have masked any association.

Although only considered in two studies, temporality may be an important factor when considering social support in long term conditions. We cannot infer causality in cross sectional designs, but prospective designs may also be problematic as a bi directional association between social support and glycemic control may exist. Elevated HbA1c may well result in increased social support. This may be particularly true with functional support where elevated HbA1c may result in help seeking and receipt of support; elevated HbA1c is less likely to result in structural measures such as marriage. In order to optimally investigate this association, a prospective cohort design is needed to measure multiple dimensions of social support at the time of diagnosis and the change in social support over time. These studies will allow us to further allude to the active component of social support and to the directionality of the association.

Associations between social support and glycemic control varied depending on the measurement of social support. Multidimensional assessments of social support may better represent the complex multi-factorial nature of social support and the multiple and interacting components that influence health. In accordance with previous research, composite measures were more predictive of biomedical outcomes than less complex measures (Holt-Lunstad et al. 2010). Furthermore, the consistent association between social support and health in the wider literature may indicate that our review failed to detect the active component(s) of social support, crucial for its effective functioning.

In type 2 diabetes, improvements in self-management, psychological functioning and biomedical outcomes are seen following formalized support interventions; support provided, for the most part, by strangers (van Dam et al. 2005). Naturally occurring relationships (e.g. friends and family) may exert a greater influence on health than support provided by health care professionals (Holt-Lunstad et al. 2010) or strangers (Edens et al. 1992). Evidence provided in this systematic review is based entirely on naturally occurring (informal) social relationships. Such support may be more prominent

in the life of an individual than organized support sessions, and able to exert a greater and sustained influence. This said, the utilization of naturally occurring social relationships (spousal support and family and friend support) in formalized interventions found mixed results (van Dam et al. 2005). Spousal support was beneficial for obese women with type 2 diabetes when attending diabetes education programs (Wing et al. 1991) but in a similar study, attendance of culturally tailored education with family or friends offered no improvement in glycemic control when compared to attending alone (Gilliland et al. 2002).

We expect that social support may vary across the course of disease, perhaps being beneficial only when individuals are in need and receptive to aid. This may, in part, explain the consistent relationship between social support and mortality seen in the literature (Holt-Lunstad et al. 2010). In type 2 diabetes we may expect social support to be more relevant with disease progression. Most of the studies included relatively healthy individuals, not experiencing life threatening conditions or end stage diabetes complications. The majority of studies recruited patients from primary care and outpatient settings; these individuals may have sufficient social support and there may be a bias against patients lacking social support who may not be attending clinics. This may lead to an underestimation of the effect of social support. Illness may also result in poorer or more restricted social relations as a result of physical confinement or disability. Sampling from community ambulatory clinics may exclude such individuals.

There is also a tendency to assume that all social relationships are supportive, but the notion that support impacts negatively upon health outcomes, including chronic disease self-management, has been previously reported (Gallant 2003). Our review did not take into account the quality of relationships. Negative support (hostility, criticism and harassment) can be counterproductive and more predictive of outcomes than positive aspects of social relationships (Clark and Nothwehr 1997).

There is evidence that social support may be a clinically relevant factor on the pathway to glycemic control. Four studies (two not included in the review) document evidence for an indirect association between social support and HbA1c, mediated by self efficacy, adherence (Nakahara et al. 2006, Mayberry and Osborn 2012), self care behaviors (Osborn et al. 2010, Fortmann et al. 2011) and depression (Fortmann et al. 2011). Many studies statistically adjusted for established risk factors. This may underestimate the effect of social support on glycemic control, since there is evidence that at least some of the impact of social support on HbA1c is mediated by these factors.

One of the strengths of conducting systematic reviews is that future designs may be improved by highlighting the limitations of existing research. This systematic review, although inconsistent in findings, highlights important conceptual and methodological barriers when reviewing the expansive and heterogeneous social support literature.

Concerns relate to the use of non standardized measurements of social support with varying validity and reliability. A multitude of social support measures exist with no 'gold standard' assessment tool available. In 30 studies, 21 different measures of social support were used. The heterogeneity between measures poses problems when comparing and reporting studies. The need to standardize social support measures is necessary for the a) progression of the evidence base b) communication to stakeholders of diabetes care and c) development of interventions. Social risk factors are challenging to measure and validate, as constructs are often difficult to define and quantify (Hidalgo and Goodman 2012). In social epidemiology research in chronic disease, we may need to use qualitative research to identify important forms of support and the conditions under which it is delivered to inform the development of standardized measures. It is important to establish whether a valid standardized measure assesses what it is designed to in diverse

populations. In health disparities research, standardized measures may sometimes not be appropriate across cultural and social domains. Less rigid, semi-structured interviews may be favorable when studying a construct such as social support. These often take into account gender and cultural variations whilst acknowledging there is something fundamental about social support regardless of these factors.

There was also high variability across studies in the measurement and definition of HbA1c, particularly amongst studies using categorical measures of HbA1c. Measuring HbA1c categorically is nowadays less seen in the diabetes literature. HbA1c is measured on a continuum to internationally accepted measures (IFCC) (Jeppsson et al. 2002). The definition of poor glycemic control ranged from 6.5% to 11.5% (48 mmol/mol to 102 mmol/mol) across studies irrespective of national guidelines. This makes comparisons across studies particularly difficult and reduces the probability of identifying trends in the literature.

3.6 **Conclusion**

The findings of this systematic review indicate tentative evidence for a potentially important role for informal support sources in glycemic control in individuals with type 2 diabetes. There is need for consensus and standardization of social support measures to build an evidence base from the literature.

3.6.iv Practice implications

The multiple resources for social support should be openly discussed with patients in healthcare settings. Males and females may utilize and benefit from social support in

different ways and this must be taken into consideration. Physicians should explore informal support sources if a patient is struggling with their self care. Diabetes care teams could encourage informal and available social support from family members before more formal support interventions are implemented.

This chapter has systematically reviewed the evidence for an association between social support and glycaemic control in type 2 diabetes. The next chapter will consider the role of the social neighborhood environment in health and its relevance to type 2 diabetes.

Chapter 4 The Neighbourhood

4.1 **Synopsis**

The aim of this chapter is to describe another social construct, the social neighbourhood environment. The environment in which we live is also an important determinant of health outcomes and this has significant implications for public health policy. In this chapter, I consider whether there is any validity for measuring neighbourhood factors at an individual and area level (Figure 13) as independent risk factors for poor glycaemic control

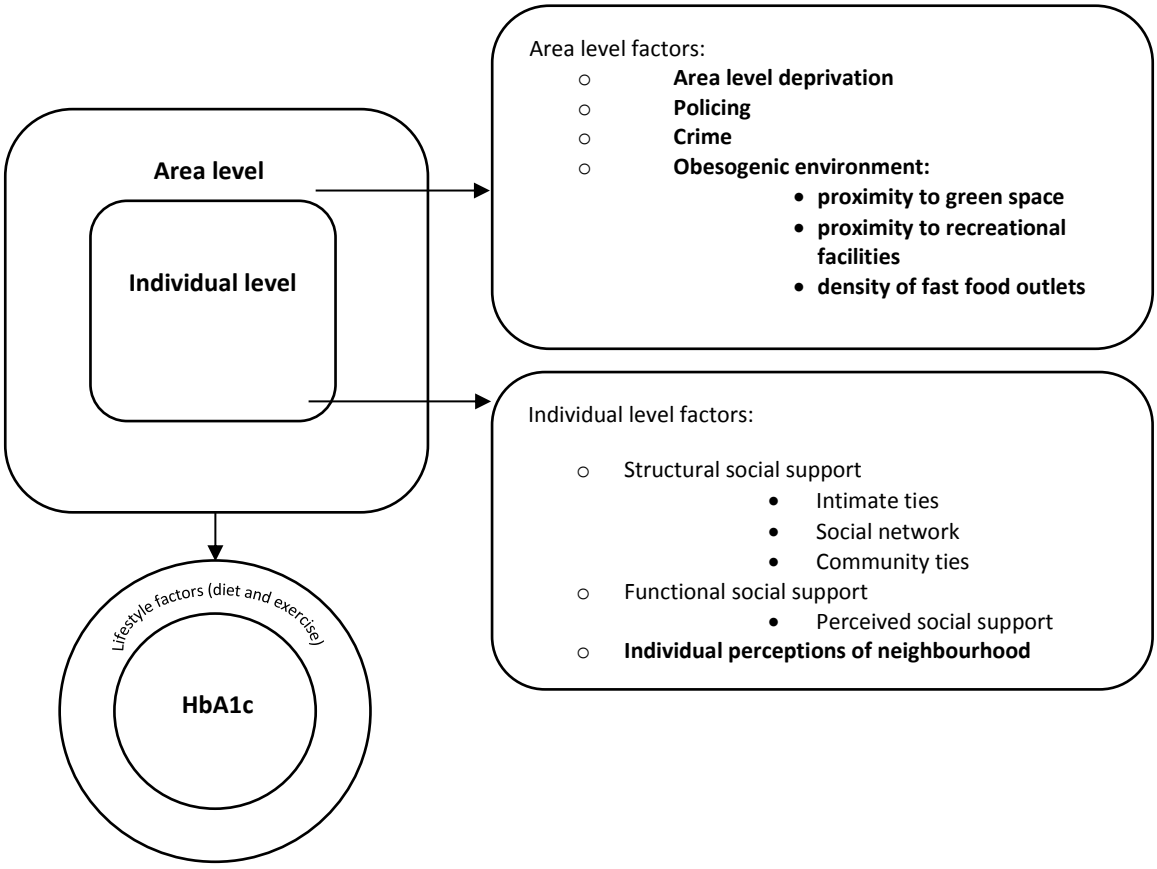


Figure 13 The proposed epidemiological model of the social determinants of HbA1c in type 2 diabetes (the variables under study in this chapter are highlighted)

4.2 **Introduction**

Sociologists and social geographers recognise that the neighbourhood environment has a pivotal role in shaping the life of an individual. The last decade has witnessed a growing literature investigating the association between area of residence and health, the geographical context in which health disparities emerge and the mechanisms by which the neighbourhood environment might impact upon health. This is evidenced by an increasing number of studies reporting geographical inequalities in health behaviours, morbidity and mortality and reporting associations between neighbourhood characteristics and health. Researchers recommend that policies aimed at reducing health inequality need to target the environment where people live in addition to the characteristics of the individuals themselves. Governments now recognise this, and the report 'Healthy Lives, Healthy People' (Department of Health 2010) emphasises the significance of environments conducive to leading healthy lifestyles.

4.3 **Conceptual challenges**

There are theoretical and methodological challenges when measuring the neighbourhood context and its relationship with health (Cummins et al. 2007, Cummins et al. 2005a). A first issue is the definition of a 'neighbourhood' or, more appropriately, the geographical area relevant to health. These have not yet been consensually defined and to add to the problem, the terms neighbourhood, community and area are loosely and inter-changeably used to encompass the space in which an individual lives. There are several possible definitions of the neighbourhood. A broad definition is that the neighbourhood environment is 'all that is external to the individual' (Papas et al. 2007). Bernard and colleagues further conceptualise neighbourhoods as 'providers of resources related to population health and to the production of health inequalities' (Bernard et al. 2006). Another construct is that the neighbourhood has two interrelated components: i) aspects

of the geographical area in which individuals reside such as deprivation and ii) a site containing resources such as supermarkets or pharmacies.

Although these definitions are geographically anchored they are not particularly precise. A more precise measurement is the use of administratively defined areas which serve as proxy markers of an individual's neighbourhood. However, these might not be consistent with how residents themselves define their neighbourhood which may be in terms of proximity to family, other social contacts or neighbourhood resources (Guest and Lee 1984). The definition of a neighbourhood might further be dependent on individual characteristics, for example, an individual who relies on public transport may have a smaller neighbourhood environment than someone who owns a car and for some purposes, the definition might be dependent on individual hypotheses and outcomes under study. For example school catchment areas may be relevant for child outcomes and administratively defined boundaries might be most appropriate when hypotheses involve policies.

There is a call for a clearer theoretical framework on which to base neighbourhood research and consensus on methodological techniques and the measurement of neighbourhood characteristics. There is heterogeneity in the current measures which poses problems for the accurate synthesis and progression of the neighbourhood literature. As a result, researchers have been unable to allude to variables of the environment with the most prognostic significance. Furthermore, some single unit neighbourhood measures (for example deprivation) may be inadequate when investigating a complex multi-factorial and multi-level construct. Another limitation of this research is that most studies use cross-sectional data which, unlike prospective studies, do not allow for the study of causality. Multi-level analyses, however, are becoming commonplace (O'Campo 2003). It must also be recognised that neighbourhoods are not static constructs. They do not have fixed characteristics, but respond to societal processes

such as economic and demographic changes and fluctuations in migration (O'Campo 2003), this further adds to the complexity of this area. In order to strengthen inferences regarding the magnitude of the effect of the neighbourhood on health these issues need to be addressed.

4.4 **Neighbourhood and health**

Macintyre and colleagues identify five neighbourhood features that may influence a resident's health (Macintyre et al. 2002).

1) physical features shared by all residents, such as quality of air or drinking water.

2) the availability of healthy environments at home, work and play such as housing, non-hazardous working environments and safe play areas.

3) services provided, publicly or privately, to support people in their daily lives such as education, street cleaning, policing, welfare services or voluntary agencies.

4) socio-cultural features of neighbourhoods such as political, economic, ethnic and religious history, community integration and crime.

5) the reputation of an area: how an area is perceived both by residents and non-residents.

Neighbourhoods possess both physical and social attributes which may affect the health of the population (Diez Roux and Mair 2010). Of the five neighbourhood features proposed by Macintyre and colleagues (physical features, availability of healthy environments, services provided to support individuals in their daily lives, socio-cultural features and the reputation of an area), features 2 to 5 constitute social aspects, although

it should be noted that physical and social attributes are not mutually exclusive. For the most part, composite measures of deprivation such as the Index of Multiple Deprivation utilise measures of social and physical attributes. For this thesis, deprivation will be considered as a social neighbourhood factor in accordance with previous research (Cummins 2005). A conceptual framework of the neighbourhood social environment in this thesis can be seen in Figure 14. I will consider the following: objective, area level factors: i) neighbourhood deprivation, ii) policing, iii) violent crime and iv) the obesogenic environment and subjective, individual level factors: i) residents' perception of the neighbourhood. It is important to consider the independent effects of both objective and subjective measures as objective, area neighbourhood level factors can be characterised independently of residents' perceptions (Weden et al. 2008) and the two do not necessarily reflect each other.

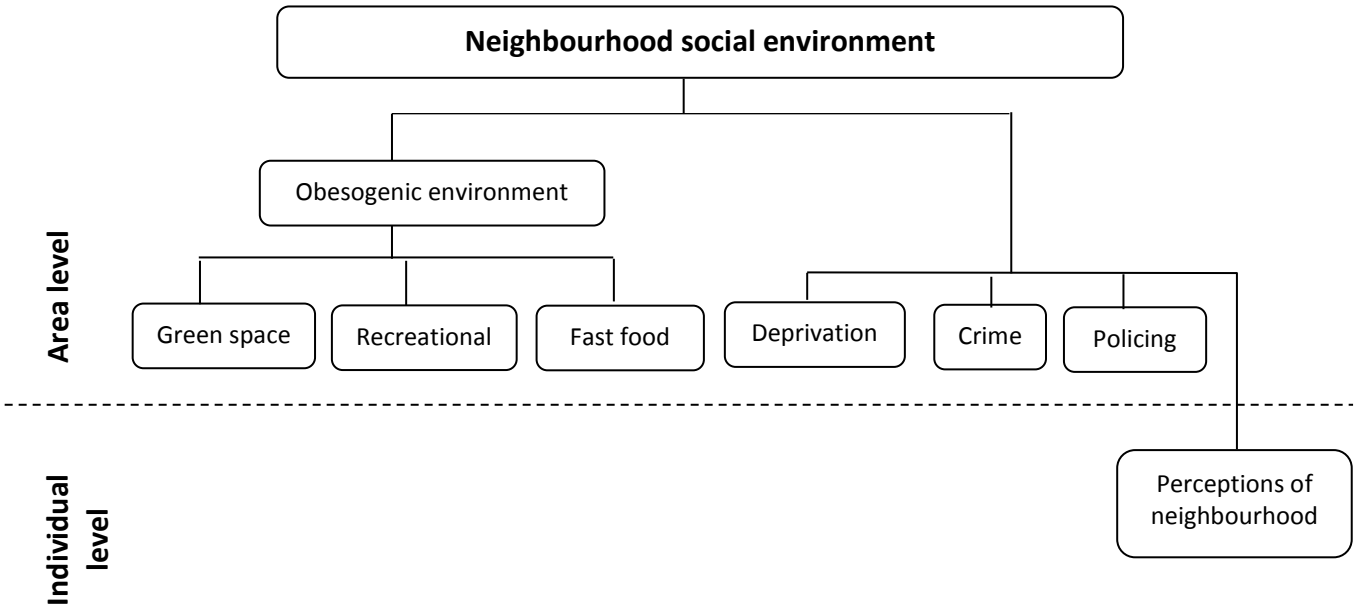


Figure 14 Theoretical framework used to describe the social neighbourhood environment in this thesis

4.4.i Neighbourhood deprivation

Neighbourhood deprivation (objectively measured neighbourhood socio-economic status) is an important determinant of health disparities independent of individual characteristics

(Cummins et al. 2007). There have been a range of measures used to capture area level deprivation. Early work was dominated by single- or multiple-item indices of census measures of socio-economic status at administratively demarcated local areas (Riva et al. 2007), but composite measures of deprivation across multiple domains (for example, employment, education, health and crime) are now more widely used. Most studies use markers of neighbourhood disadvantage (such as deprivation indices), as opposed to neighbourhood advantage (health promoting aspects of the neighbourhood, for example community levels of aspiration). Other measures of neighbourhood deprivation include researcher based observations of neighbourhood conditions and the presence or density of facilities as a proxy marker, for example, fast food restaurants, recreational facilities and medical care facilities.

Neighbourhood deprivation (as measured by national censuses or indices of deprivation) is associated with adverse health outcomes; cardiovascular and coronary heart disease (Roux et al. 2001), breast cancer incidence, respiratory function or illness, insulin resistance syndrome (Diez Roux et al. 2002), type 2 diabetes (Cox et al. 2007) and excess mortality (Pickett and Pearl 2001, Freedman et al. 2011). Neighbourhood deprivation is also associated with cardiovascular risk factors: hyperlipidaemia, BMI (Smith et al. 1998), hypertension and glycaemic control (Geraghty et al. 2010, Laraia et al. 2012). These associations remain after controlling for individual socio-economic status (Pickett and Pearl 2001) and are often stronger in females than males (Freedman et al. 2011).

In cross-sectional studies, neighbourhood deprivation has been consistently associated with participation in health related lifestyle behaviours (diet, physical activity and smoking) (Stimpson et al. 2007, Cubbin et al. 2006). In one study of the general population in Sweden, living in an area of high deprivation was associated with higher odds of smoking, physical inactivity and obesity, independent of demographic variables and

individual socio-economic status when compared to individuals living in areas of more moderate deprivation (Cubbin et al. 2006). Similarly, in the UK, a cross-sectional analysis of participants in the 2008 East of England Lifestyle Survey found that neighbourhood deprivation was associated with unhealthy lifestyles, independent of individual socioeconomic factors. Individuals in the higher quintiles of deprivation were more likely to smoke, drink alcohol and less likely to consume five servings of fruit and vegetables on five or more days of the week (Lakshman et al. 2011). In one of the few prospective studies, the Black Women's Health Study, women living in areas of neighbourhood deprivation in the US had higher mean BMI and energy intake, were more likely to smoke and drink alcohol, were less physically active and were more likely to have a family history of type 2 diabetes than women living in less deprived neighbourhoods (Krishnan et al. 2010). Neighbourhood deprivation was associated with an increased risk of the development of type 2 diabetes over the 12 years follow-up after controlling for demographic, individual socio-economic status and lifestyle factors. These studies suggest that neighbourhood deprivation influences health outcomes independently of individual level socio-economic status, an important finding for public health policy.

On the other hand, there are a few studies that defy this general trend and demonstrate a morbidity and mortality 'resilience' (Tunstall et al. 2007). Those who resist the effect of a situation to which most would succumb, are referred to as 'resilient'. This indicates that for some, there may be factors which act as a buffer and weaken the consistently observed detrimental effect of socio-economic disadvantage on health. An important finding, however, is that although relative to areas of similar deprivation 'resilient' areas experience lower morbidity and mortality, their rates remain elevated compared to the British average (Tunstall et al. 2007).

Resilience reflects an 'overachievement', in health terms, of certain neighbourhoods. That is, some neighbourhoods experience better health outcomes than predicted given their deprivation status. In a cross-sectional study of 354 local authorities in the UK, life expectancy was strongly associated with deprivation (Doran et al. 2006). However, some deprived local authorities overachieved whilst some affluent areas underachieved. Overachieving authorities were characterised by large ethnic minority populations, high levels of unemployment, overcrowding, rented housing and lone parenthood. Similarly, in their study of 39 chronically deprived parliamentary constituencies in the UK, Cairns at al. (2012) report health resilience to be associated with greater availability of social housing, employment in higher occupational grades and higher concentrations of ethnic minorities. A high concentration of ethnic minority groups may implicate the ethnic density effect where low concentrations of an individual's ethnic group are associated with worse health outcomes (Halpern and Nazroo 2000) (this is described in detail in Chapter 8). Better health may result from higher levels of social cohesion, culturally tailored environments and a reduction in the frequency of adverse events, for example, racism (Bécares et al. 2009, Whitley et al. 2006).

The use of aggregate neighbourhood measures as the sole measure of neighbourhood characteristics is a controversial topic in epidemiology and sociology studies. Although these measures are readily available and serve as proxies for some attributes, the omission to measure more specific factors and examine their independent effects on health remains a limitation (Diez Roux 2003). Often proxy markers are used for complex measures which are intuitively understood, such as area level deprivation, but are difficult to directly measure with accuracy (Pickett and Pearl 2001). Another dilemma is whether aggregate variables are measures of area level characteristics in their own right or whether they are simply summaries of individual level factors (Roux 2001). Macintyre and colleagues (2002) comment that neighbourhood effects are often a 'black box of somewhat mystical influences on health' (Macintyre et al. 2002). They, and others,

suggest that analyses should use more specific environmental and neighbourhood domains (crime, policing, access to healthcare) in the place of global summary measures to capture neighbourhood attributes, and refrain from classing 'neighbourhoods' as just another single feature in an epidemiological web of causation (O'Campo 2003).

4.4.ii Crime and policing

Neighbourhood disorder (characterised by composite measures of vandalism, crime, loitering, noise, police officers) has been repeatedly associated with adverse health (Ross and Mirowsky 2001, Stafford et al. 2007b). However, only a limited body of research associates specific objective measures of neighbourhood disorder such as crime and policing with poor health outcomes. At the individual level, fear of crime (an individual's perception) has been independently associated with mental health problems, psychological distress, reduced outdoor physical activity, high blood pressure and poor self-rated health (Middleton 1998, Stafford et al. 2007a, Ross 1993, Parkes and Kearns 2006), but it is unknown whether objective but specific measures (rather than composite measures) are associated with adverse health outcomes. It seems plausible to suggest that neighbourhood crime and policing would influence psychological distress, perceptions of safety and the ability to live independently. High levels of crime, and/or, low policing levels may reduce the size of an individual's neighbourhood, making them reliant on a smaller spatial area reducing opportunities for healthy eating and physical activity.

4.4.iii Perceptions of neighbourhood and health

Individual perceptions of neighbourhood environments may be as, if not more, important than objective neighbourhood measures (Wilson et al. 2004, Haan et al. 1987). Subjective

neighbourhood measures are individual appraisals of neighbourhoods (Gary et al. 2008, Parkes and Kearns 2006) which may, or may not, reflect observable reality. Although objective measures may appear more accurate, an individual's own appraisal might better reflect how much their neighbourhood environment affects them. Neighbourhood perceptions may elicit psychological or stress responses that may be associated with health. It has been suggested that perceptions mediate the association between objectively measured constructs and health outcomes (Weden et al. 2008).

Subjective measures reflect a complex interaction between neighbourhood characteristics which may be undetected in objective measurements. For example, if an area experiences high crime levels but has few derelict buildings and good access to local amenities, then an individual's perception of such a neighbourhood may be favourable, despite some adversity. Objective measures would not reflect this. Additionally, the neighbourhood environment may not affect all residents in the same way. Certain demographic groups may be more susceptible to the influence of their surroundings (Powell-Wiley et al. 2013), females and the elderly for example. Like objective neighbourhood measures, subjective measures have been examined as single items or as composite measures (Weden et al. 2008, Gary et al. 2008). In this thesis a composite measure is used, the Neighbourhood Perceptions Questionnaire, but individual items such as fear of crime are also common.

Negative perceptions of one's neighbourhood are associated with poor physical and mental health including self-reported health status (Poortinga 2006, Ellaway et al. 2001, Wilson et al. 2004). The most consistently reported finding is the association between neighbourhood perceptions and obesity (Poortinga 2006, Powell-Wiley et al. 2013, Catlin et al. 2003), mainly in North American studies. A cross-sectional analysis of the Dallas Heart Study found that individuals with the least favourable perceptions of their neighbourhood physical environment were 25% more likely to have a BMI higher than 30

kg/m^2 than those with the most favourable perceptions. This association was independent of demographic and socio-economic variables, length of residence and the physical environment (Powell-Wiley et al. 2013), but perceptions of neighbourhood violence and social cohesion were not associated with obesity. Another cross-sectional study of 1,504 adults in contrasting neighbourhoods in Canada found that individuals with negative perceptions of their neighbourhood environment were 1.5 times more likely to report chronic health conditions and were more likely to self-report 'fair / poor' health or emotional distress (Wilson et al. 2004) when adjusting for demographic factors, socio-economic status, lifestyle variables and BMI. Similarly, cross-sectional data from the 1996 British Crime Survey (n = 16,090) reported that perceived fear of crime explained differences in self-rated health independently of health behaviours and individual and household socio-economic variables (Chandola 2001). Although the evidence is overwhelmingly cross-sectional, one longitudinal study in Alameda County (n = 6,928,) reported excessive noise, traffic, inadequate lighting and limited access to transport to be independently associated with a decline in physical impairment over 1 year in older adults (Balfour and Kaplan 2002), controlling for individual, socio-economic, biological and behavioural risk factors.

4.5 **The obesogenic environment and health**

Although a social construct, the obesogenic environment reflects the physical neighbourhood environment and is associated with health. It includes the built environment, environmental exposures, food and recreational resources, existence and quality of natural spaces and housing quality (Diez Roux and Mair 2010) and is strongly influenced by globalisation. The term 'built environment' encompasses aspects of an individual's surroundings which are man-made or modified, as opposed to naturally occurring features.

The built environment may influence individuals' health decisions as well as pose barriers to maintaining a healthy lifestyle. The term 'obesogenic environment' refers to elements in the environment that support weight gain. These environments, which foster low levels of physical activity and ease of access to energy-rich foods, are thought to be one of the most important determinants of obesity and related diseases, such as type 2 diabetes. Three markers of the obesogenic environment will be used in this thesis i) fast foods, ii) recreational facilities and iii) green space (Figure 14).

Lifestyle 'choices' of individuals may be constrained by structural neighbourhood conditions. The assumption is, that if a community has a lack of, or unkempt green space, limited recreational facilities, or long distances to areas conducive to exercise, then residents are less likely to engage in physical activity. Distance is generally perceived as a barrier to use, with individuals in close proximity having more opportunities for use, less travel time and lower travel costs. Similarly, if healthy food choice is limited and fast food outlets are in high supply, then it may be more challenging to follow a healthy diet. Differences in the availability and access to healthy foods and recreational facilities are potential determinants for the social patterning of type 2 diabetes (Stringhini et al. 2012) but evidence for the association between proximity to resources and frequency of use remains inconclusive and understudied, especially in long term conditions.

4.5.iv Fast food outlets

Purchasing from fast food restaurants is becoming increasingly commonplace, particularly in western societies. Such food is up to 65% more energy dense (energy content per unit weight of food) than the average diet, and frequent consumption is positively associated with BMI (Prentice and Jebb 2003).

Living in close proximity to, or within a high density of fast food outlets, is associated with obesity. In their systematic review, Leal and Chaix (2010) reported a consistent association between increase in fast food restaurant density and increased body weight in six out of nine studies. A large cross-sectional study in the USA reported that a 1 standard deviation increase in the density of fast food outlets was associated with a 7% increase in the prevalence of overweight/obesity (Li et al. 2008). These analyses were independent of individual level and neighbourhood socio-demographic characteristics. A longitudinal study of older adults reported that neighbourhoods with low walkability and a high density of fast food outlets were associated with increases in systolic and diastolic blood pressure independently of resident- and neighbourhood-level socio-demographic variables (Li et al. 2009). The most logical mechanism of this association is unhealthy dietary choice. In Ontario, Canada, cross-sectional analyses found that students living more than 1 kilometre (km) from a convenience store had higher Healthy Eating Index scores (a US measure of diet quality assessing compliance to federal dietary guidelines with a higher score indicating healthier eating) than those living within 1km. Students attending schools with three or more fast food outlets within a 1km radius had lower healthy eating scores than those further away (He et al. 2012).

A smaller, but still significant, body of literature has found no association between access to fast food restaurants and health (Jeffery et al. 2006, Lopez 2007). This is unsurprising due to the heterogeneity of measures used and because researchers are often limited by availability of data. Firstly, a distinction must be made between fast food outlets and full service restaurants, the latter is associated with reduced BMI (Leal and Chaix 2010). Full service restaurants typically offer healthier food, are more expensive and are located in less deprived neighbourhoods, they may also be associated with more favourable health outcomes, but not all studies make this distinction. Secondly, conceptual definitions for the food environment vary widely (from 400m to 8km from residential address (Papas et al. 2007)) and, more recently, it has been suggested that the definition of a

neighbourhood should equate to an individual's 'shopping neighbourhood': areas that can be accessed in a 'reasonable amount of time' (Zick et al. 2009). However, a conceptual challenge remains. The shopping neighbourhood varies between demographic group, access to transportation and geographical location so this definition adds little to advance consensus on methodological concerns.

Furthermore, the causal direction of the association between fast food outlets and health related outcomes, primarily obesity, is inconclusive. A bi-directional association may exist: i) an increase in fast food restaurants may cause an increase in obesity or ii) increased prevalence of obesity in certain areas may cause an increase in fast food outlets. Having reviewed the evidence for the former, there is also evidence that an increase in fast food restaurants reflects an increasingly obese population, rather than being a direct cause of obesity (Jeffery et al. 2006). Fast food outlets (as opposed to full service restaurants) are typically located in areas where obesity prevalence is high (more deprived areas). In Melbourne, Australia, more deprived neighbourhoods have 2.5 times more fast food outlets (Reidpath et al. 2002) and in England and Scotland, McDonald's restaurants are typically located in more deprived areas (Cummins et al. 2005b). However, in Glasgow, UK, the density of out-of-home food outlets was not associated with area level deprivation (Macintyre et al. 2005). The authors suggest that food outlets in Glasgow are located in areas of high potential custom in the centre of the city which are also the most affluent areas. These analyses included both restaurants and fast food outlets which are associated with more affluent and more deprived areas respectively which may have masked any association. These conflicting findings further add to complexities of neighbourhood research and may indicate that international, or even national, comparisons are just not possible in this area of research.

4.5.v Recreational facilities and green space

The provision of green open space and recreational facilities, may provide important places for individuals to be active, especially in urban areas (Coombes et al. 2010). At present in England, it has been estimated that only 40% of males and 28% of females are meeting the minimum recommended levels of physical activity (150 minutes of moderate-intensity physical activity per week) (NHS Information Centre 2008).

Access to green space and recreational facilities is associated with more favourable health status. Green environments are associated with lower blood pressure and levels of obesity but increased rates of circulatory disease and all cause mortality (Mitchell and Popham 2008). A large cohort of 574,840 participants in Ontario, Canada reported that individuals living in areas with higher densities of green space had reduced non-accidental mortality rates over a follow-up period of almost two decades (Villeneuve et al. 2012). Analyses were adjusted for income, marital status, ambient air pollution and contextual neighbourhood characteristics but the authors emphasise the likelihood of residual confounding by socio-economic or lifestyle factors. Richardson and Mitchell similarly reported that, at ward level, as green space increased, cardiovascular and respiratory disease mortality rates decreased in males but not in females (Richardson and Mitchell 2010). These associations were independent of age, income deprivation, air pollution and country. A possible explanation for this finding is that males and females experience and utilise green space in different ways. Females are underrepresented in their use of green space and are less likely to engage in vigorous physical activity in green spaces (Cohen et al. 2007). Social and psychological barriers have also been identified in the use of green spaces in females. Females report concerns about their safety when visiting green spaces alone and feel safer in obviously managed areas. Compared to males, females also report feeling significantly more uncomfortable in neglected or derelict areas and have less preference for remote settings than males (O'Brien 2005).

One of the mechanisms of the green space - health association is engagement in physical activity; an established risk factor for physical and mental ill-health. A systematic review of 50 studies published between 1998 and 2005 found that 80% observed an association between the presence of physical activity resources and recreational facilities and physical activity levels of residents (Kaczynski and Henderson 2008). In a cross-sectional analysis of the US Multi-Ethnic Study of Atherosclerosis, a higher density of recreational resources (within 1-5 miles of home address) was associated with an increased probability of engaging in physical activity independently of demographic and socio-economic factors (Roux et al. 2007). A similar association was seen in Perth, Australia, where proximity to public open spaces was associated with increased walking (Giles-Corti et al. 2005). After adjustment, individuals with very good access to large and attractive public open spaces were 50% more likely to self-report high levels of walking. However, Hoehner and colleagues found no association between living within 5 minutes of green space (objective and subjective measurements) and meeting physical activity guidelines in Missouri and Georgia, USA (Hoehner et al. 2005). Similarly in the UK, Hillsdon and colleagues reported no association between distance to green space and self-reported physical activity (Hillsdon et al. 2006).

Methodological discrepancies make drawing conclusions difficult. Inconsistencies may be due to the assessment (self-reported or actual) of access to green space or recreational facilities or due to the specific socio-demographics and location of a geographical setting. The perception and use of green space may also differ between inner-city settings and rural areas. Green spaces in cities are busier and more widely used but also more frequently the scene of crime and antisocial behaviour. In an inner city, green space could be a marker of affluence, but this may not be the case in city suburbs or the countryside. Furthermore, recreational facilities in large cities may be more expensive than in rural areas, but possibly also more accessible. For convenience, individuals may also choose to utilise green space or recreational facilities close to their place of work. For these

individuals, resources within their residential neighbourhood may be less important. The validity of generalising findings across national or international scales may therefore be questionable.

4.6 **The neighbourhood environment and type 2 diabetes**

Despite increasing interest in the association between the neighbourhood environment and health, research has only recently begun to address this question in type 2 diabetes. Existing research has largely focused on neighbourhood factors which influence the risk of developing type 2 diabetes rather than considering factors associated with its course. This was reaffirmed by a recent systematic review of the social determinants of health outcomes in type 2 diabetes which only identified 3 studies that considered the 'neighbourhood and built environment' (Walker et al. 2014).

It is well known that the incidence and prevalence of type 2 diabetes is increased in deprived neighbourhoods (Connolly et al. 2000, O'Kane et al. 2010, Mueller and Berger 2012) but it is less well known whether the area in which an individual lives is an important determinant of glycaemic control. To the best of my knowledge, only 2 studies, both cross-sectional, have investigated the association between neighbourhood deprivation and glycaemic control. In the DISTANCE Study, a large cohort (n = 19,804) in Northern California, increasing deprivation, measured using the neighbourhood deprivation index, was associated with poor glycaemic control independent of individual socio-economic status (Laraia et al. 2012). Again, in California, when registry data of 7,288 individuals was matched to US census data using Geographic Information Systems (GIS), low income neighbourhoods were associated with higher HbA1c in adults with type 2 diabetes, independent of individual socio-economic status (Geraghty et al. 2010). Longitudinal data are needed to test the causal direction of these associations and it is of

interest to investigate whether this association holds outside of the US. This is one of the primary aims of this thesis.

The reason for the lack of studies reporting associations between the neighbourhood and glycaemic control may be because any association is likely to be indirect. Two mediators are commonly cited i) behavioural risk factors (physical activity, diet, smoking, ability to recover from stress) (Diez Roux 2003) and ii) repeated exposure to stressful situations.

Lifestyle modifications such as frequent exercise and healthy diet are cornerstone to optimal diabetes self-care. Living in a neighbourhood with limited or unsafe places to exercise and inadequate access to healthy food may pose a significant barrier for the self-management of the disease. I have previously reviewed the evidence for an association between the neighbourhood and health behaviours. It is consistently reported that neighbourhood conditions and access to facilities (recreational facilities, green space and fast food outlets) are associated with lifestyle and cardiovascular risk factors (Giles-Corti and Donovan 2002, Li et al. 2008). These factors are also associated with risk of type 2 diabetes. The Multi-Ethnic Study of Atherosclerosis Neighbourhood Study found that better neighbourhood resources (healthy food and access to physical activity) were associated with a 38% lower incidence of type 2 diabetes independent of age, gender, family history of diabetes, ethnicity, income and education (Auchincloss et al. 2009). Similarly, greater resources for physical activity have also been associated with lower insulin resistance independently of demographic and socio-economic factors and family history of diabetes (Auchincloss et al. 2008).

However, research in individuals with type 2 diabetes is significantly more limited. A cross-sectional study of 7,830 participants with type 2 diabetes participating in the US Translating Research Into Actions for Diabetes (TRIAD) study found that the perception of

neighbourhood problems (crime, trash, litter, lighting at night, and access to exercise facilities, transportation, and supermarkets) was associated with diabetes behaviours and biomedical outcomes. Individuals who perceived the most problems reported higher levels of smoking, lower participation in physical activity, poorer blood pressure control and self-rated health status after adjustment for socio-demographic and socio-economic variables, comorbidity, duration or diabetes and objective neighbourhood socio-economic status (Gary et al. 2008). At the time of writing there are no published studies that investigate the association between the recreational and fast food environments with self-care behaviours or glycaemic control in type 2 diabetes. This is a primary aim of this thesis and a secondary aim is to investigate whether any association between the neighbourhood and HbA1c is mediated by lifestyle variables.

Another proposed mediator of the association between the neighbourhood and glycaemic control is physiological stress. Neighbourhood crime, lack of safety, anti-social behaviour and low social cohesion could all be sources of stress for residents which may subsequently impact upon HbA1c. The environmental fear concept serves as a framework which underpins the associations between environmental fear and health. Repeated exposure to environments that are deemed threatening may speed up the malfunctioning of physiological systems (Taylor et al. 1997). When a situation is perceived as stressful, physiological and behavioural responses are initiated which lead to allostasis (the process of achieving homeostasis) and adaptation. However, if a threat response is repeatedly stimulated, as may be the case with on-going exposure to stressful environmental triggers, then recovery from this reaction may become impaired. Allostatic load refers to the 'wear and tear' the body experiences as a result of repeated physiological responses to stressful situations (McEwen and Stellar 1993). The physiological stress response and development of allostatic load can be seen in Figure 15. Increased blood glucose levels may be a response to high allostatic load (Langelaan et al. 2007).

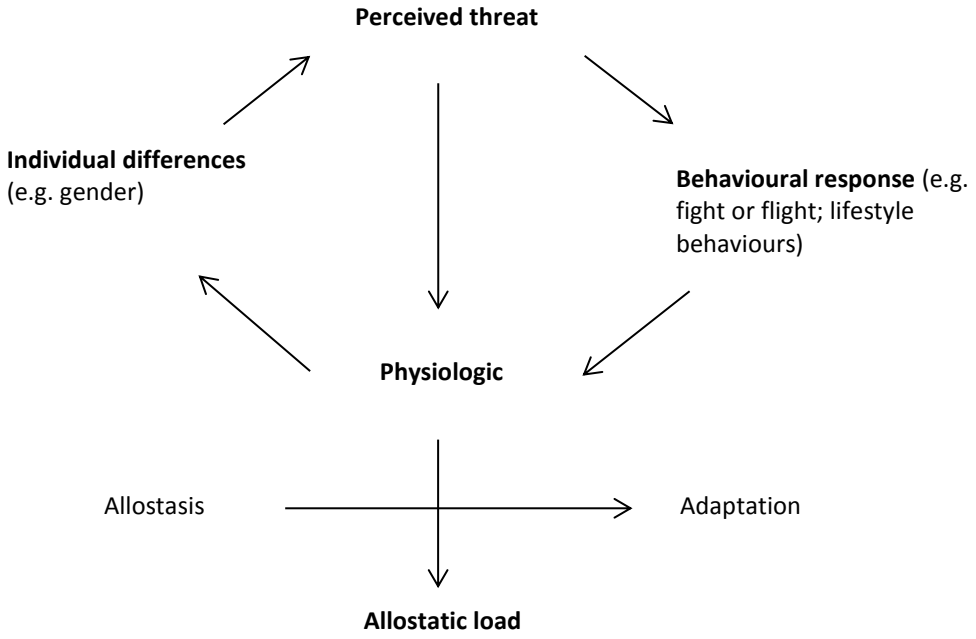


Figure 15 The associations between perceived threat and allostatic load (Adapted from McEwan 1998)

4.7 **Conclusion**

Research into neighbourhood characteristics and health tends to examine the association between either the social or the physical environment and health, using either individual or area level measures (Weden et al. 2008, Stafford and Marmot 2003). Few studies consider both concepts simultaneously. Furthermore, evidence for the importance of neighbourhood factors in the self-management of type 2 diabetes is limited. Population level behavioural change is necessary for primary prevention of the epidemic of type 2 diabetes and for secondary prevention of diabetes complications. However, behavioural change is often complex and dependent on many variables at both individual and area levels, and may not be sustainable in unsupportive environments. Examining whether the neighbourhood context influences diabetes outcomes is not only of academic interest, the neighbourhood has many modifiable targets for intervention and for innovation in national housing and social policies, as was achieved with no smoking policies in public

buildings. But despite exponential growth of multi-level studies, we still lack clear direction in policy implications and intervention in this area of research. The association between neighbourhood context and health outcomes, and the mechanisms of action, have important implications for public health and the reduction of health disparities. These factors may be most strongly implicated in concentrations of poverty and social disadvantage, areas where a disproportionate representation of type 2 diabetes, high levels of poor diabetes control and increased economic burden associated with the disease exist.

This review of the literature surrounding the neighbourhood effects on health suggests that the neighbourhood environment could be a modifiable target of intervention however, more evidence is needed of the association with diabetes control.

The next chapter describes the methodology used in this thesis.

Chapter 5 Methodology

5.1 **Synopsis**

This chapter describes the study methodology which was chosen to optimally study the social determinants of glycaemic control in individuals with newly diagnosed type 2 diabetes. Participants were recruited from primary care in 3 inner-city boroughs of South East London. The setting was multi-ethnic and socio-economically diverse and captured variations in healthcare provision. Social variables were chosen to reflect the expansive and multi-faceted nature of the social determinants of health and multi-level statistical analyses enabled the identification of the most significant social determinants of glycaemic control whilst accounting for relevant confounding and clustering within GP.

5.2 **Introduction**

My review and conceptual understanding of the literature is that the social context of an individual is an important prognostic variable which shapes individual lives and opportunities, but social factors are complex, often multifaceted and difficult to define. Methodological issues have been identified since the rise of interest into the social determinants of health (O'Reilly 1988). Criticisms relate to the lack of definition of social variables, the use of inappropriate designs, measures and statistical methodology with lack of controlling for relevant confounding variables. These issues are listed in our recent systematic review (Stopford et al. 2013) and described in Chapter 3.

When this conceptual framework is applied to type 2 diabetes, evidence for the importance of the social determinants of glycaemic control is scarce. In this thesis it was important to use an observational design to i) determine whether social support variables and neighbourhood level factors (at both individual and area levels) were associated with glycaemic control, ii) to investigate the mechanisms of any association and iii) inform future interventions for this population group. It was also important not to over-simplify social variables by using few composite measures. For this reason, a variety of social variables were chosen to reflect the multifaceted nature of social factors and to identify key social components in the management of type 2 diabetes.

5.3 **Design**

This thesis is embedded within the South London Diabetes (SOUL-D) study, a prospective cohort with 1 and 2 years follow-up. SOUL-D is a NIHR Programme Grant funded observational study. The primary hypothesis was to investigate the association between

depression and HbA1c. It was developed because i) the evidence for an association between depression and HbA1c was mainly cross-sectional and reports small effect sizes and ii) to identify the biological, psychological and social mechanisms explaining the association.

A cohort study uses an observational design to investigate the association between an exposure and an outcome. At the onset of the study the exposures are defined but the outcomes have not yet occurred. Participants are followed-up over a period of time to assess outcomes (Hennekens and Buring 1987). Cohort designs can be either prospective or retrospective in nature but both designs classify participants according to the presence or absence of exposure. At the initiation of a prospective cohort the relevant exposures may or may not have occurred but the outcomes will not have occurred. In retrospective cohort studies both the exposure and the outcome of interest have already occurred at the start of the study.

The strength of prospective cohort studies is that they provide evidence for the temporal sequence of events which is a key factor in assessing bidirectional associations and causation. Using a prospective cohort design also allows for the study of multiple explanatory factors and multiple outcomes simultaneously. Prospective cohort studies reduce the potential for selection bias on the basis of outcomes, as at the start of a study these have not yet occurred. Selection bias can arise when the inclusion of cases into the study are associated with the outcome of interest (Hennekens and Buring 1987). Selection bias is often most evident in case-control studies as exposure and outcome have both occurred at the time participants are selected for inclusion in the study.

The main bias of the prospective cohort design is losses to follow-up. If loss to follow-up is large or if loss to follow-up is skewed towards a particular risk factor, for example if more

individuals with depression are lost to follow-up than those without depression, then the validity of study results may be questioned. Another bias is nonparticipation. In cohort studies, only a proportion of those eligible agree to participate. The demographic characteristics of those who choose to participate may differ from non-participants, in their motivation, attitudes and access to health. Additionally, since large samples are followed-up for long durations (e.g. 10 – 20 years), studies are time consuming and expensive to run (Hennekens and Buring 1987).

The use of other study designs such as a RCT, cross sectional or case-control studies would be inappropriate. RCTs represent the 'gold standard' for assessing causality but they do not allow for the study of multiple explanatory variables. Furthermore, their experimental design and allocation of exposure groups might not be best suited to the study of naturally occurring constructs such as the social determinants of health. Some social constructs, such as social support can be artificially induced. Doing so, might help us to understand formal forms of social support for example, support from a healthcare provider or spouse involvement at a health education event. Artificially inducing social support may not replicate or reflect naturally occurring everyday forms of support in the home or neighbourhood. Furthermore, the socio-ecological nature of social determinants cannot be easily controlled under experimental conditions at the standard required for a RCT. The effect of crime levels on health outcomes would be one such example and ethical considerations would also be a concern. In type 2 diabetes, the literature on the social determinants of glycaemic control is scarce and so a RCT is premature. Cross-sectional designs examine data on exposure and outcome at a single time point, therefore they cannot establish the temporal association between exposure and outcome. The hypotheses in this thesis could have been tested using a case control design, but again, exposure and outcome have already occurred at entry into the study, so no causal inferences can be made. Additionally, case-control studies are susceptible to bias due to

the allocation of cases and control based on their exposure status (Hennekens and Buring 1987).

5.4 **Study population and case definition**

All individuals registered at participating GP surgeries in three adjacent South London boroughs; Lambeth, Southwark and Lewisham (LSL), who fulfilled the following eligibility criteria, were invited to take part in the study.

Eligibility Criteria

Inclusion Criteria:

1) Adults with a clinical diagnosis of type 2 diabetes mellitus defined according to the WHO criteria (WHO 1999) (see Chapter 1, Figure 2 for definition) in the preceding 6 months. Diabetes duration was calculated from the date of diagnosis as stated in the medical records.
2) Adults aged between 18 and 75 years.

Exclusion Criteria:

1) Patients not fluent in English as the reliability of psychiatric interviews and questionnaires may be low.
2) Temporary residents of LSL and those outside the catchment area as we aimed to follow-up participants over 2 years.

3) Severe mental illness such as bipolar disorder, psychosis, learning disability, dementia, severe personality disorder or schizophrenia.
4) Terminal illness or advanced disease as it was not considered ethical.
5) Severe diabetes complications defined as registered blind, kidney dialysis or above the knee amputation which are very unlikely in a newly diagnosed sample.

5.5 **Setting**

Adults with type 2 diabetes were recruited from GP practices across the London boroughs of Lambeth, Southwark and Lewisham (LSL) (circled in Figure 16) which have a multi-ethnic and socio-economic diverse resident population of approximately 0.7 million (Census 2011). The sampling frame included all 138 general practices in the three boroughs to capture variations in health care provision. In the UK, all GP practices are required to maintain an up-to-date diabetes register.

Lambeth is the second largest of the inner London boroughs, with a total population of 303,100 (Census 2011). It has the fifth highest population density in the UK. Over 60% of the residents of Lambeth are not of UK origin and over 150 languages are spoken. The black and minority ethnic population account for 38% of the total population of Lambeth, significantly higher than the London average of 28.9% (Census 2001). Deprivation scores across Lambeth wards are higher than average for the UK. Sixteen out of the 21 wards in Lambeth are in the top 20% of the most deprived wards in England (IMD 2007).

Southwark has a population of 288,300 (Census 2011). The black and minority ethnic population accounts for 37% of the total population in the borough. Southwark is the 26th

most deprived borough in England (out of 354 local authority districts) and is the 9th most deprived borough in London (Southwark Analytical Hub 2008).

Lewisham is the third largest of all London boroughs with a population of 275,900 and is highly residential in nature (Census 2011). Like Lambeth and Southwark, the black and minority ethnic population make up a similar proportion (34%) of residents. Lewisham is the 39th most deprived borough in the UK, placing it in the 20% most deprived areas within England (IMD 2007).

These three boroughs were chosen as they are local to Kings College Hospital. They have a multi-ethnic and socio-economically diverse population, and are areas where a disproportionate burden of type 2 diabetes exists. These boroughs have a large black community which is understudied in research. Compared to the rest of the UK, there are high rates of migration to these boroughs, and the demography may increasingly represent large cities across Europe and North America.

Figure 16 Map of the London boroughs

5.6 **Sample size estimation**

A prospective power calculation for regression analyses was conducted using nQuery Advisor (Elashoff 2007) to determine the sample size required using an alpha of 0.01, 90% power and a conservative explained variance of 1.5%. The desired sample size is 961. Assuming a 30% drop out, the required sample size is 1373 (Option 4). Other calculations were considered (Options 1, 2 and 3) as acceptable alternatives in case recruitment fell behind target or attrition rates were higher than expected (Table 4). In order to account for clustering within GP, the sample was multiplied by the variance inflation factor (VIF):

$$VIF = 1 + (n - 1)p$$

where n is the average number of participants in each cluster and p is the intraclass correlation (ICC). The ICC quantifies how strongly individuals in each cluster resemble each other. It is typical that ICC values are between 0.01 and 0.05 for clustering at GP level. With an ICC of 0.05 and an average cluster size of 10.38, the sample size was multiplied by a factor of 1.47 making the preferred sample size n = 2018. This sample size was not achieved over the course of this PhD (Option 4) Consequently Option 2 (alpha of 0.01, 90% power and a conservative explained variance of 5%) was chosen.

Table 4 Sample size estimation

	Option 1	*Option 2*	*Option 3*	*Option 4*
Significance level (α)	0.01	0.01	0.01	0.01
Number of prior covariates (A)	15	15	15	15
Total variance explained	0.05	0.02	0.02	0.02
Number of covariates to add (B)	1	1	1	1
Increase in variance explained with addition of B to A	0.05	0.05	0.02	0.015
Power (%)	90	90	90	90
N	272	451	718	961
Total n (allowing for 30% drop out)	389	645	1026	1373
Total n (accounting for the effect of clustering within GP)	572	949	1502	2018

Shaded area = selected sample size

5.7 **Ethics**

Ethical approval was given by the King's College Hospital Research Ethics Committee (ref: 08/H0808/1) and by Lambeth, Southwark, Lewisham and Bromley Primary Care Trusts (ref: RDLSLB 410).

5.8 **Method of sampling and recruitment**

GP recruitment

All 138 GP surgeries across the participating South London boroughs were invited to participate in the study. Surgeries were invited to participate by e mail followed by a phone call regardless of patient list size, numbers of registered patients with diabetes or number of practising GPs. Surgeries that expressed interest were given a presentation before giving consent.

Participant recruitment

Once a practice had consented, the electronic diabetes register was screened using the study inclusion and exclusion criteria in order to identify potentially eligible patients. Screening was repeated at 6 monthly intervals during the recruitment phase. Each surgery sent letters to all eligible patients identified by the search describing:

i. The rationale of the study
ii. What the study would involve: completion of self-report questionnaires, a physical assessment and a fasting blood test, and follow-up period
iii. Biomedical data sharing with GPs
iv. Confidentiality

Potentially eligible patients were contacted by telephone to provide additional information about the study and to invite them to volunteer. Research assistants then arranged an appointment with patients to conduct the baseline interview. Where

possible, this appointment was scheduled with their routine diabetes screening to reduce duplication of data collection for the Quality and Outcomes Framework (QOF). This facilitated good relationships with practice staff.

5.9 **Procedure**

At baseline, all eligible participants who agreed to an appointment were met by a research assistant at their GP surgery. Participants were given the study information sheet (Appendix II) and research assistants answered any questions. Participants gave written informed consent (Appendix II). The diagnosis of type 2 diabetes was validated at recruitment by a review of the medical records for an entry confirming the clinical diagnosis of type 2 diabetes. Inclusion and exclusion criteria were verified again at this stage using a standardized form (Appendix II). Research assistants administered a standardized data collection schedule: medical history, clinical examination, blood test under fasting conditions (no food or drink, other than water, for 8 hours preceding the appointment) and self-report social and psychological questionnaires (Appendix III). Appointments were conducted by trained research assistants using pre-specified standard operating procedures.

At 12 months post-recruitment, all participants who were alive were contacted and invited to return for a further appointment with a research assistant. The baseline assessment was repeated. No variables from this time point are used in this thesis.

At 24 months post-recruitment the same procedure was repeated. Variables collected at this follow-up point can be found in Table 5.

Multiple contact attempts by post and by telephone were made by research assistants and a range of appointments were offered to participants. Participants received a telephone call or text reminder the day preceding their appointment. After not attending an arranged appointment 3 times, over 3 months from due date, the participant was labelled as non-contactable for that follow-up time point.

Strategies to maximise data collection were as follows:

1) If a participant remained in the study catchment area but could not attend a follow-up appointment, questionnaires and blood request forms were sent by post to the participant for them to complete and return. All remaining physical data were recorded from medical records if available for that time point.

2) If participants had moved out of the study area and contact could be made, questionnaires were sent by post to participants for completion at home. Contact was made with new GP surgeries to obtain biomedical data from medical records.

3) Where no contact with participants could be made, biomedical data was collected from patients' medical records.

4) If participants wished to withdraw, they were asked whether existing data could be retained and whether biomedical data could be collected from their medical records. This would help to keep missing data to a minimum and maximise outcome data.

5) If a participant had died during the course of the study, death certificates were requested to establish cause of death.

Table 5 Variables used in this thesis (collected routinely as part of the SOUL-D study and data obtained from external sources)

	Baseline	Year 2	Data from other sources
Demographic	Age / gender Ethnicity Employment status NS-SEC	 Educational attainment English as a second language	
Social support	Marital status Social network Community ties Perceived social support		
Neighbourhood	Neighbourhood perceptions		Index of Multiple Deprivation Violent crime statistics Data on the number of police officers Distance to green space Distance to recreational facility Density of fast food restaurants
Biological / psychological / behavioural	BMI (kg/m^2) Blood pressure (mm Hg) Waist circumference (cm) HbA1c (mmol/mol) Total cholesterol: HDL ratio Macrovascular complications Medication PHQ-9 SDSCA diet SDSCA exercise Smoking status	 HbA1c (mmol/mol) Medication SDSCA diet SDSCA exercise	

NS-SEC: UK National Statistics Socio-Economic Classification; BMI: body mass index; HDL: high density lipoprotein; SDSCSA: Summary of Diabetes Self-Care Activities; PHQ-9: Patient Health Questionnaire-9.

5.10 **Measures**

The measures used in this study had already been set by the larger programme of which this PhD is a part. This put constraints on what could be assessed and subsequently address the methodological limitations identified by the systematic review. This was particularly the case for social support variables. There was significantly more flexibility with the choice of objective neighbourhood variables which were chosen on the basis of my literature review. These were obtained from external sources where the only constraint was the availability of data. In this section, only measures that are relevant to the hypotheses investigated in this thesis are described. This thesis uses data from SOUL-D at baseline and at year 2. The complete SOUL-D data collection schedules at these time-points can be found in Appendix III and a summary of variables used in this thesis is found in Table 5.

5.10.i Explanatory variables

Social Support

Structural social support

i) Marital status. Participants were asked about their marital status: married, cohabiting, single, divorced or widowed. For analyses 4 main groups were used: i) married or cohabiting, ii) separated or divorced, iii) widowed and iv) single.

ii) Social network. Participants were asked to report the frequency of social contacts, by type, in a typical week, this could be face-to-face or telephone contact. Participants were given a list of individuals including: siblings, in-laws, other relatives, close friends,

neighbours, boss/supervisor, co-workers, helping professionals, other acquaintances or a member of a group of organisation (Lin et al. 1999), and were asked to answer yes or no to each individual on the list. The range of social contacts was 0 – 10.

iii) Community ties. Participants were asked to record their participation in community activities, groups, organisations or social clubs across seven domains including faith related groups, job related associations, recreational groups, fraternal services, civic and political groups and senior citizen groups (Lin et al. 1999). Respondents indicated whether or not they were associated with any of the given groups and were given the opportunity to provide additional groups not listed. The total number of affiliated clubs or groups reflects the overall strength of community ties.

Functional social support

i) Perceived social support. Participants were presented with 5 standardised hypothetical situations (Lin et al. 1999). Participants were asked whether they would be able to receive help or assistance on a regular basis (at least 2-3 times a week) should they need it. Situations included: needing someone to lend you money to pay bills or help you get along, someone to help with your daily routine if you are not feeling well, someone to talk to about something that is bothering you, company if you feel lonely or just want to talk, someone to make you feel good, loved or cared for. Possible responses were: 1 = no, 2 = yes with difficulty or 3 = yes. The range of the perceived social support scale was 5 – 15. Cronbach's alpha coefficient assesses the degree to which items on a particular measure assess the same underlying attribute. Values range from 0 – 1. Higher values indicate greater reliability. The perceived social support scale demonstrates good internal consistency (alpha coefficient = 0.84) (Lin et al. 1999).

Neighbourhood factors

Area level neighbourhood factors studied are i) neighbourhood deprivation, ii) violent crime rates and iii) policing and iv) the obesogenic environment measured using 1) distance to sports facilities and 2) distance to green space and 3) density of fast food outlet. All area level data were matched to participant postcode at baseline. The individual level neighbourhood variable is perceived neighbourhood disorder.

Area level

Data collected were obtained from central government departments, local authorities and public sector agencies. Data were provided free of charge or were obtained from online information sources in the public domain.

The aim was to collect data at Lower Layer Super Output Areas (LSOA) for all study sites (Lambeth, Southwark and Lewisham). However, where this was not possible, data were obtained at the smallest geographical area for which it was available. This was the case for total police numbers which were obtained at Census Area Statistics (CAS) wards as opposed to LSOA for other study variables.

LSOA: These are the smallest administratively defined geographical areas in England and comprise of between 1000 and 3000 persons and between 400 and 1200 households. The 2011 Census reported the average population of an LSOA to be 1614 people and 672 households (Census 2011).

CAS wards: There are 8850 CAS wards in England and Wales, each is the size of 4-5 LSOAs.

i) The Index of Multiple Deprivation (IMD 2010) (McLennan 2011) is an aggregate measure of relative neighbourhood deprivation reflective of the circumstances and lifestyles of residents. The IMD uses 38 indicators of deprivation across seven domains: income, employment, health and disability, education skills and training, barriers to housing and other services, crime and living environment. The weightings used for each of the seven domains can be found in Table 6. A direct comparison to the IMD does not exist so it is not possible to directly compare this measure with another source. However, there are high correlations between indicators within the domains indicating construct validity, the measurement of the same latent construct.

Table 6 Domain weight used to calculate IMD 2010 (Greater London Authority 2011)

Domain	**Weight**
Income deprivation	22.5%
Employment deprivation	22.5%
Health deprivation and disability	13.5%
Education, skills and training deprivation	13.5%
Barriers to housing and services	9.33%
Crime	9.33%
Living environment deprivation	9.33%

The data were obtained at LSOA, the smallest geographical area at which these data are available. Participant postcodes at baseline were matched to LSOA which was subsequently matched to IMD score and ranking. The ranking of the IMD score is expressed across a national range (1 being the most deprived and 32482 being the least deprived LSOA in England).

ii) Violent crime: violent crime is classified as violence against the person, sexual offences and robbery (Metropolitan Police 2013). Data were obtained from the Metropolitan Police but sexual offences data are withheld. Total violent crime rates were obtained monthly for the boroughs of Lambeth, Southwark and Lewisham at LSOA level throughout the recruitment phase (January 2009 - November 2011). Total crime data were matched to participant postcodes at the date of recruitment. Higher values represent higher levels of violent crime.

iii) Number of police officers: the number of police and community support officers (CSO) serve as a proxy marker for neighbourhood social disorder, replicating previous studies (Stafford et al. 2007b). Police officers and CSOs (introduced as part of the Police Reform Act (2002) to address low level crime and increase police visibility) represent the visual police presence of an area. The Metropolitan police report that higher numbers of community support officers reflect areas of higher demand, risk and complexity. The total number of police and community support officers was calculated from the Metropolitan Police website where data are publicly available. Participant postcode was matched to ward which was subsequently matched to total number of police and CSOs.

The obesogenic environment

Green space, recreational facilities and fast food outlets were chosen as markers of the obesogenic environment. All facilities were mapped based on their recorded location in the United Kingdom Ordnance Survey Points of Interest Classification Scheme (contains Ordnance Survey data© Crown Copyright and database right 2013) (Ordnance Survey 2012) (Appendix IV). This database provides information on the geographical location of land use, coded according to type. Each feature is assigned a national grid coordinate which allows it to be viewed as a geographical location. The

precision of all coordinates is at least 1 metre (Ordnance Survey 2012). The following definitions were used:

1) Green space: areas in which physical activity could potentially be undertaken and are free to use: commons, parks, picnic areas and playgrounds.

2) Recreational facilities: facilities used to participate in indoor or outdoor sports, facilities which have indoor gymnasiums or facilities with specialist equipment for one sport. Recreational facilities usually require a fee to use: climbing facilities, golf ranges and courses, gymnasiums, sports halls and leisure centres, sports grounds, stadia and pitches, squash courts, swimming pools, tennis facilities and velodromes.

3) Fast food outlets: a retailer selling hot food ready for consumption on, or off, the premises: fast-food and takeaway outlets, fast-food delivery services, fish and chip shops and bakeries. These are in contrast to a full service restaurant.

Geographical Information Systems were used to compute distance from participant postcodes to green space and recreational facilities and to compute the density of fast food outlets in an individual's proximate neighbourhood. The proximate neighbourhood was delineated as the area within 400 metres along the road network from participant postcode. This distance equates to a 5 or 6 minute walk and is comparable to other research in inner city locations (Pikora et al. 2002, Simon et al. 2008). Calculations took place in 3 main steps:

1) The spatial locations of participant home addresses were determined by geocoding (finding associated coordinates: longitude and latitude / easting and nothing) full participant postcode. Postcodes were geocoded, in groups of 100 postcodes, using a

free access website (doogal.co.uk). To ensure accuracy, one in every 10 postcodes was geocoded again using a similar free to access website, where only one postcode could be entered at a time (Johnson 2013).

2) Green space, recreational facilities and fast food outlets were identified using the Ordnance Survey Points of Interest User Guide. Points of Interest allow for the identification of facilities in the built and natural environment. The numeric codes for each point of interest were used to find their geographical locations within ArcGIS 9.2 Geographical Information System Package (ESRI, California) (Appendix IV).

3) Geocoded coordinates and points of interest were mapped using ArcGIS. These were overlaid on a base layer. Microsoft Bing Hybrid Maps were used as the basemap layer for this analysis (Esri, California). It is a high performance basemap layer that is continuously updated and contains information on the road network.

The distance from participant postcode to the nearest green space and recreational facility was calculated along the road network in metres with accuracy to 10 decimal places. This figure was rounded to the nearest metre. The density (number) of fast food restaurants within an individual's proximate neighbourhood (400m along the road network) was computed.

Individual level

i) Perceived neighbourhood problems. Participants' perceptions of neighbourhood problems such as crime, access to exercise facilities and litter was measured using an adapted version of the scale used by Gary and colleagues (Gary et al. 2008). Eight items were included. Participants were asked: 'thinking about where you live, how

much of a problem is each of the following: crime, access to exercise facilities, rubbish and litter, lighting at night, access to transportation, access to nearby supermarket, vandalism/graffiti, safety?' Each item had four possible responses (very serious problem, somewhat serious problem, minor problem and not a problem). Responses to each item were summed to create a summary score. Higher scores indicate perception of fewer neighbourhood problems.

Biological variables

i) BMI was calculated as the weight in kilograms (kg) divided by the square of the height in metres (m^2). Standing height was measured to the nearest millimetre (mm), without shoes, using a Seca 222 wall-mounted vertical rule. Weight was measured to the nearest 0.1kg without outdoor clothing or shoes using Seca 877 analogue weighing scales (Seca, Birmingham, UK).

ii) Waist circumference was used to measure central fat distribution and degree of abdominal obesity. Waist circumference was measured to the nearest 0.5 centimetre (cm) at the mid-point between the lowest rib and the iliac crest.

iii) Blood pressure was recorded using an electronic sphygmanometer (BP742, Omron® Healthcare, Inc.). Readings were taken when the patient was seated and had rested for at least five minutes.

iv) Total cholesterol: high density lipoprotein cholesterol ratio (TC:HDL ratio) was calculated from total cholesterol and HDL values as a measure of serum lipid profile. Fasting lipids were measured using the Siemens Adiva 2400 analyser (Siemens

Diagnostics, Frimley, UK), detection limits of the assays were: total cholesterol 0.01 mmol/L and HDL cholesterol 0.1 mmol/L.

v) Microvascular disease was defined as a presence of neuropathy, retinopathy or nephropathy. Neuropathy was assessed by measuring vibration perception threshold (in Volts (V)) using a neurosthesiometer. The device was placed on the big toe and participants were asked to report when they could feel a vibration. This was repeated three times, the lowest voltage for each toe was recorded. Being unable to detect a voltage of >25V indicates significant neuropathy and these participants were coded as neuropathic. Retinopathy was recorded from the participants eye screen at diagnosis which was performed by the Diabetes Eye Complication Screening (DECS) service. Data were coded as i) retinopathy absent: no retinopathy detected at screening or ii) retinopathy present: treated retinopathy (e.g. laser or photocoagulation), non-sight threatening retinopathy (e.g. background, mild / minimal pre-proliferative or mild / moderate non-proliferative) or sight-threatening retinopathy (e.g. maculopathy, moderate/severe pre-proliferative). Nephropathy was assessed at diagnosis of diabetes, using the urinary albumin creatinine ratio (ACR). Ratios of ≥3 were positive and <3 were negative.

5.10.ii Potential mediators

A mediator is a variable that may explain (in full or in part) the association between an independent and dependent variable. In contrast to direct associations, mediators are on the causal pathway of the association between risk factor and outcome. Mediators differ from moderators. Generally, moderators are variables that affect the strength or direction of associations between an independent and dependent variable. Most commonly these might be age, gender or ethnic group (Section 5.10.iii).

Diabetes self-care behaviours

i. Diabetes self-management was assessed using the Summary of Diabetes Self-Care Activities Measure (SDSCA)(Toobert et al. 2000), an 11-item self-report questionnaire that assesses the frequency of diabetes self-care behaviours across five domains: diet (4 items); exercise (2 items); blood glucose testing (2 items); foot care (2 items) and smoking (1 item). In this thesis the diet, exercise and smoking subscales were used as they reflect healthy lifestyle behaviours which are of interest as mediators in this thesis.

For diet, the SDSCA assesses adherence to general diet (2 items) and adherence to dietary recommendations (2 items): eating five or more servings of fruit and vegetables a day and eating high-fat foods (reverse scored). Exercise levels were assessed by asking participants on how many of the last seven days they participated in at least 30 minutes (continuous) of physical activity and how many days they participated in a specific exercise session. Smoking status was ascertained by asking patients whether they had smoked a cigarette in the past 7 days. This question required a binary (yes / no) response.

Responses for all other subsections of the SDSCA are recorded on a likert frequency scale. Responses range from 0 – 7 (number of days per week). Higher scores indicate higher levels of self-care.

When the scale comprises a small number of items (<10), the Cronbach's alpha coefficient can often be small. In this case it is often better to report the mean inter-item correlation. The optimal range for the inter-item correlation is 0.2 to 0.4 (Briggs and Cheek 1986). The SDSCA demonstrates acceptable internal reliability assessed

using inter-item correlations (mean = 0.47). The internal reliability for the diet subscale was relatively low (Toobert et al. 2000).

5.10.iii Potential confounders

Confounding variables are independent factors which are associated with the exposure and, independent of that exposure, the outcome of interest. Confounding factors, by definition, should not be an intermediate step on the causal pathway between exposure and outcome (mediation). When potential confounding is not taken into account in the statistical test, this may lead to an overestimation (and sometimes underestimation) of the association between a risk factor and an outcome which weakens the statistical validity of observed outcomes of interest (Hennekens and Buring 1987). Study design and statistical analyses must address these issues. Stratification, multivariable and multi-level analyses are statistical approaches used to control for confounding in this thesis. Detailed rationales for the use of confounders are described in the methodology sections in results chapters 7 and 8.

<u>Demographic confounders</u>

i) Age (years). Ageing is defined as the gradual biological impairment of normal function, as a result of changes made to cells (mitotic cells, such as fibroblasts and post-mitotic cells, such as neurons) and structural components (such as bone and muscle). These changes would consequently have a direct impact on the functional ability of organs (the heart, kidney and lungs), biological systems (the nervous, digestive and reproductive system) and ultimately the organism as a whole. Age is associated with most diseases and risk factors and should always be considered as a confounder in an association (Hennekens and Buring 1987). It is known that social variables vary according to age, as an example, social networks decrease in size with increasing age (Ajrouch et al. 2001).

ii) Gender (male or female). Similar to age, gender is associated with most diseases and risk factors and is therefore considered as a confounder in analyses (Hennekens and Buring 1987). Most social factors are associated with gender. For example, females report larger social networks and closer confiding ties whilst males report smaller networks and their spouse as their closest emotional contact (Shye et al. 1995).

iii) Ethnicity. Participants self-reported their ethnicity. Main subgroups were classified as White, Mixed, Black, Asian, Chinese or other ethnic group and were based on 2001 UK Census methods (HMSO 2001). For analysis three main groups were used: White, Black and South Asian / other.

iv) Employment status. Participants self-reported their employment status as: i) full time employment ii) part time employment iii) unemployed iv) medically retired/ unemployed v) retired vi) full time carer or vii) student. For analyses, 3 main groups were used: i) employed ii) unemployed or iii) retired.

v) Socio-economic status. Social class was measured using the UK National Statistics Socio-Economic Classification (NS-SEC). The NS-SEC is theoretically based on variations in employment relations and conditions. It is derived from the respondent's occupational title, distinguishing between employers and employees, and responsibilities over the workforce. Within employers, large scale employers (25 or more employees) are distinguished from small employers and own account workers (less than 25, or no employees). Employers are distinguished on their service relationship and labour contracts. Managers and professionals have a service relationship with their employers and hold a position with a high degree of trust and authority. These occupations are often long term and hold prospective elements. Employees involved in routine work often have labour contracts specifying discrete amounts of labour done under supervision and receive wages calculated on a time basis (Chandola and Jenkinson 2000). The NS-SEC classes can be distinguished on the

basis of work autonomy and the differences in employment relations such as terms of remuneration and job promotion prospects. This measure replaces prior classifications including the Registrar General's Social classification. The five-class version of the NS-SEC has the following classes: 1) Managerial, administrative and professional occupations 2) Intermediate occupations 3) Small employers and own account workers 4) Lower supervisory and technical occupations and 5) Semi-routine and routine occupations. This version was used in analyses for two reasons: i) to reduce the number of independent variables in analyses leading to type 1 errors and ii) to reduce the number of categories containing small participant numbers.

vi) Educational attainment. This was a self-report measure with the following options: i) no qualifications, ii) GCSE or Ordinary level, iii) ONC/BTEC/HND/NVQ/C&G, iv) A levels or Highers/Baccalaureate, v) Higher educational qualification below degree level (i.e certificates or diplomas from universities) and vi) degree or higher degree level. To improve distribution, 4 main categories were used: i) no qualifications, ii) qualifications up to GCSE or Ordinary level iii) qualifications up to A Level iv) higher degree or above.

vii) English as a second language. Participants were asked whether English was their second language i) yes or ii) no. For participants bilingual in English and another language, English was coded as their first language.

Psychological confounders

i) Depression status. Depression was assessed using the Patient Health Questionnaire – 9 (PHQ-9) (Spitzer et al. 1999), a 9 item self-report questionnaire. The PHQ-9 scores the presence and severity of depression symptoms according to the Diagnostic and Statistical Manual for Mental Disorders IV (DSM-IV). Each of the 9 symptoms is scored on a scale from 0 (not at all) to 3 (nearly every day). The questionnaire produces both a

continuous (range 0-27) measure of depression and a categorical measure of depression (Kroenke et al. 2001). A score of ≥ 10 represents the likelihood of depression.

Biological confounders

i) Previous macrovascular event. This was defined as a history of: myocardial infarction, coronary artery bypass graft, cerebrovascular accident and carotid or limb revascularisation. This was self-reported and validated from medical record review.

ii) Diabetes medication. All prescription medication was recorded from medical records. Participants were classified into two groups: i) individuals who were prescribed oral antidiabetic drugs or insulin and ii) individuals not taking any diabetes medication.

5.11 **Main outcome**

i) HbA1c at 24 months. HbA1c is a marker or glycaemic control which is associated with the risk of developing diabetes complications (Cheng et al. 2009, Khaw et al. 2004, Turner et al. 1998).

Glycated haemoglobin (HbA1c) is a laboratory test that reflects glycaemic control (average plasma glucose concentrations) over the 8 to 12 weeks preceding the test as the proportion of haemoglobin that is glycated depends on the amount of glucose in circulation. HbA1c assesses the amount of glucose attached to the N terminal of the β chain of haemoglobin. Haemoglobin A comprises over 90% of most adult haemoglobin and is variably glycated by the non-enzymatic attachment of sugars. The level of

glycation is not linear with time, 50% of the value reflects 30 days prior to the test as a red blood cell has a life of 12 weeks.

As a test, HbA1c has many attractions: no dietary preparation, such as fasting, is required, the blood sample can be collected at any time, it is relatively unaffected by acute stress and the sample is stable at room temperature for at least a week (Wass et al. 2011). The limitations of HbA1c are that it does not always reflect a true average blood glucose as it is a proxy measure over 12 weeks. It may also be inaccurate in individuals with elevated haemoglobin F or with abnormal haemoglobins found in sickle cell trait.

Prior to June 2009, HbA1c assays were aligned to those used in the Diabetes Control and Complications Trial (DCCT) and were reported as a percentage. Since, a new standard specific was prepared by the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) (mmol/mol) to allow for international comparisons. The reference range for people without diabetes is 25.7 – 47.5 mmol/mol (4.5-6.5%) (Williams and Pickup 2004). For people with diabetes target values are usually between 47.5 – 58.5 mmol/mol (6.5% and 7.5%) but this must be judged on individual risk for micro- and macro- vascular complications (McIntosh et al. 2001).

Venous blood samples were drawn following an overnight fast (no food or drink other than water) for a minimum of 8 hours and were analysed at King's College Hospital Laboratory. Values were obtained using the Primus Ultra 2 Bonorate Affinity HPLC (Primus Corporation, 4231 E. 7th Terrace, Kansas City, MO 64132).

5.12 **Data management**

Data entry

IBM SPSS Statistics 20 for Windows was used for data entry. All participants were given a unique identification number. Data were input by an external agency where all clinical record forms (CRFs) and questionnaires were double entered in their entirety. No identifiable information was entered into the database.

Quality control of questionnaires

All research assistants were trained according to standardised operating procedures (SOPs). Researcher meetings were held every six months to ensure consistency in data collection and to address any difficulties encountered by existing or new research assistants. Issues that had arisen from data entry were also discussed, consensus reached and standardised solutions documented.

5.13 **Statistical Plan**

Missing data

Missing data are a problem for observational studies. Participants may not always attend all follow-up visits and questionnaires posted to participants are often returned incomplete. Inevitably, loss to follow-up also occurs. Strategies were implemented to keep the problem of missing data to a minimum. Where biomedical data were missing they were recorded from patient medical records. This was only possible when data

were available within 3 months of the scheduled follow-up date (calculated based on date of entry into the study). Multiple attempts were made to collect non-biomedical missing data by telephoning participants. Only data that would not change over time could be collected retrospectively from participants in this way, for example, gender, ethnicity and education status.

When using self-report measures missing data can often prove problematic. Imputation was used where possible. For self-report measures missing less than 20% of responses the mean of the available responses was used to calculate an overall score. This method is robust in handling item level missingness where less than 20% of items are missing in both random and systematic patterns (Fox-Wasylyshyn and El-Masri 2005). Individual questionnaires missing more than 20% of responses were excluded from analyses.

Participants missing outcome data were excluded from multivariable analyses. To ensure these individuals were typical of the whole sample: the demographic characteristics of participants excluded from analyses due to missing data were compared with the remaining sample.

Normality of data

The assumptions for statistical tests were checked. Data were checked for normality. It was found that HbA1c values at baseline were skewed so a natural log was used to transform values.

Floor and ceiling effects refer to specific problems encountered when utilising questionnaire data. A ceiling effect occurs when a large concentration of responses on

a particular measure are near, or at the upper limit of the scale. Similarly, the opposite effect can occur: a floor effect. Scale attenuation can pose methodological problems when variance on a scale is restricted. Skewed continuous questionnaire data which could not be normalised by log or other transformation, were transformed into categorical variables.

Statistical analyses

IBM SPSS Statistics 20 (IBM SPSS Inc, Chicago, IL, USA) for Windows was used for descriptive and unadjusted data analyses. Stata 11.2 Version 11 (Stata Corporation, TX, USA) was used for multi-level analyses.

Descriptive data were summarised as mean (standard deviation) or frequency (percentage). For HbA1c at baseline, the non-transformed median and interquartile range (IQR) was reported as data were positively skewed.

Next, mixed effects multi-level models were used to investigate associations between social variables and HbA1c at 2 years when accounting for clustering within GP. Clustering within GP practices is inherent in the study design. Multi-level models were used as there is a two-level nested structure: level 1 (participants) who are nested (clustered) within level 2 (GP practices). Typically, the lowest level (for example individual level characteristics) is known as level 1 and the higher level (for example GPs) is Level 2. Multi-level models do not require the same numbers of level 1 units within each higher level unit. Looking for clustering within GP practices allows for the accounting of therapist effects and an area level effect. Multi-level modelling accounts for the different levels in hierarchical data and separates the variance attributable to different levels. They allow for the exploration of several levels simultaneously (for example at the level of the individual and at the level of the service provider). If

analysis is solely carried out at the individual level without accounting for any higher level clustering, the occurrence of natural clustering within populations is ignored. Without accounting for this, the effects of predictor variables may be incorrectly interpreted in strength and direction. This may be particularly important in large cohort studies. The proportion of the variances explained by the GP was estimated using the interclass correlation. This is defined as the ratio of the variance attributable to the GP: total variance (error variance + variance attributable to patients). The ICC indicates how strongly individuals within the same GP practice resemble each other.

Initially, these models were used to investigate the association between each independent variable and HbA1c. Each independent variable was entered separately into the model accounting for GP level only. This analysis was conducted twice: i) initially for or the cohort as a whole, using all cases with data for each association and ii) secondly, using only the sample included in the adjusted multi-level analyses (cases with complete data for all covariates). Comparison of the unadjusted results of these analyses will help to establish whether there is evidence of selection bias in the restricted sample. Mixed effects multi-level models were again used to investigate the independent associations between social variables and HbA1c at 2 years as a continuous dependent variable when controlling for relevant confounding. Unstandardized regression coefficients (b), 95% confidence intervals and p values are reported. The minimal change in HbA1c considered to be clinically important and of public health significance is 6 mmol/mol. Stratified analyses were conducted when appropriate and the rationale for stratified variables is described in respective results chapters.

For any association, a factor can be a confounder and an effect modifier, a confounder but not an effect modifier, an effect modifier but not a confounder, or neither (Hennekens and Buring 1987). As previously described, confounding and effect modification are very different. This thesis uses both approaches. Confounding variables were added to regression models to control for a ‘nuisance effect’ which may

distort the association between risk factor and outcome. Stratified analyses, a technique used in analyses of associations within homogenous groups, will also be used as another method of controlling for confounding. For example, if gender is a potential confounder, then the association between risk factor, for example social network, and outcome, HbA1c, would be calculated separately for men and women. As recommended, the use of variables for effect modification will be based on previous theory and on 'eyeballing' data (Hennekens and Buring 1987). The most informative approach to presentation of stratified data is to describe effect sizes and confidence intervals for each strata.

Assumptions of (multi-level) regression models were checked. Data were checked for collinearity. Any highly correlated independent variables would not be entered into a model simultaneously as this can incorrectly lead to the identification of significant predictor variables. The linearity of associations between independent variables and HbA1c were also checked using quadratic terms to account for non linear associations. The quadratic term was only included in the final model when it was significantly associated with the outcome. If the quadratic terms were non-significant they were excluded from analyses.

Multiple testing was accounted for using Hochberg's improved Bonferroni Method (Hochberg 1988). Hochberg's procedure is more powerful than other multiple testing correction methods, but it assumes that the p-values are independent. The uncorrected p values will be reported but only discussed as significant if they reach the Hochberg threshold. If p values are significant prior to correcting for multiple testing but then lose significance after Hochberg they will be treated as trends as these findings must be interpreted with caution. All p values reported are 2 tailed.

5.14 **Discussion**

This chapter has provided an outline of the methods that will be used to test the main hypothesis which are:

i) poor social support will be associated with higher HbA1c at 2 years follow-up.

ii) adverse neighbourhood conditions will be associated with higher HbA1c at 2 years follow-up.

As the evidence for a role of social factors in type 2 diabetes is inconclusive, the most appropriate design was a prospective cohort which allowed for the explorative study of multiple explanatory variables over a 2 year follow-up period whilst controlling for relevant confounding variables. Other designs were considered but were likely to be premature (RCT) or limited by selection bias (case-control study).

The assessment of the social determinants of heath has received criticism for their 'vagueness'. The measures selected here encompass a broad range of social variables at an individual and area level and are already identified as risk factors in social epidemiology. This was necessary given the lack of evidence base in type 2 diabetes. Acknowledging the problems with the validity of self-report measures, the selected variables combined subjective and objectively collected measures. They form a comprehensive assessment by using a broad range of constructs to reflect the multifaceted and complex nature of social factors. By choosing a range of social variables the risk of residual confounding from latent social constructs is also reduced.

The statistical approaches were chosen to best answer the hypotheses under study and deal with multiple social constructs and issues with confounding variables in population studies. The approaches include: i) regression analyses which allow for the

control of multiple confounding, ii) stratification for overcoming the effect of well-known confounders iii) multi-level analyses to account for clustering within GP surgery, inherent in the study design and iv) mediation in order to investigate the mechanisms of any associations. To the best of my knowledge there have been no prospective cohort studies on the social determinants of glycaemic control utilising a multi-level approach.

The next chapter describes the baseline characteristics of individuals with a recent diagnosis (< 6 months) of type 2 diabetes and compares them with existing cohorts.

Chapter 6 Baseline characteristics of the sample

6.1 **Synopsis**

The global prevalence of type 2 diabetes is rising. With changing demographics and improvements in clinical practice, the characteristics of individuals being diagnosed with the disease are also likely to change. The aim of this chapter is to describe the characteristics of people with newly diagnosed type 2 diabetes in 3 inner-city South London boroughs and to compare these with existing data. This chapter also aims to evaluate the representiveness of participating general practices and participants and to describe attrition rates. Socio-demographic and biological data were collected by standardised clinical assessments and from medical records within 6 months of diagnosis of type 2 diabetes. From 138 general practices 96 consented to participate and from 2641 individuals diagnosed, 1805 consented to participate. This thesis includes individuals who consented to participate between September 2008 and November 2011 (n = 1447). The mean age was 56 years (±11.06); 55% were male; and 51%, 38% and 11% of the sample were white, black and south Asian/ other ethnicities respectively. The mean BMI was 31.9 kg/m^2 (± 6.50), systolic and diastolic blood pressure was 136.0 mmHg (±17.82) / 83.1 mmHg (±10.80) and the median HbA1c was 48.6 mmol/mol (IQR = 43.17 – 48.63). Compared with other newly diagnosed cohorts, data from this large representative cohort indicate that the profile of individuals being diagnosed with type 2 diabetes may be changing, with lower HbA1c but higher prevalence of obesity. These findings may help to inform recourse allocation for disease prevention.

6.2 **Introduction**

Globally, rates of type 2 diabetes are rising. The increasing prevalence is predominantly due to ageing populations and increasing levels of obesity. A high prevalence of type 2 diabetes is also seen in ethnic minority groups. With changing demographics and migration of high-risk populations, particularly in large cities, and changes in clinical practice such as improvements in screening programmes and medical management, the characteristics of individuals being diagnosed with the disease are also likely to change. Few large prospective studies have described the clinical characteristics at the diagnosis of diabetes except for the landmark UKPDS study (UKPDS 1998) and the more recent European Anglo–Danish–Dutch study of Intensive Treatment In PeOple with screeN detected diabetes in primary care (ADDITION Europe). The results of UKPDS, in particular, may not apply to current diabetes populations (Winkley et al. 2013). The UKPDS cohort was predominantly white and was recruited over 20 years ago, prior to the introduction of the Quality and Outcomes Framework (QOF), an incentive scheme introduced in 2004 which rewards GP practices according to levels of achievement on certain indicators. ADDITION Europe, although recruited more recently (between 2001 and 2006), was also a predominantly white sample which only included individuals between 40 and 69 years of age. This chapter reports on baseline data from a multi-ethnic sample with newly diagnosed type 2 diabetes from 3 inner-city boroughs of South East London.

Prospective cohort studies offer a number of advantages for evaluating an association between exposures and outcomes, however 2 main sources of bias exist: i) the effects of non participation and ii) the effects of loss to follow-up. At recruitment, the cohort must be representative of the population from which it is drawn. In a prospective cohort the decision to participate cannot be based on the outcomes (as these have not yet happened), however participation may correlate with demographic, biological, psychological and social factors associated with outcomes. In general, in a prospective cohort, selection bias is less of a concern than in other designs such as case control

studies. Participant attrition is more of a problem, if loss to follow-up is large (30-40%) then the validity of findings may be questioned (Hennekens and Buring 1987). Researchers may try to minimise drop out at the expense of participation rates.

The main aims of this chapter are i) to describe the demographic and clinical characteristics of a cohort with newly diagnosed type 2 diabetes and compare these with existing cohorts, ii) to compare the baseline characteristics of participants and non-participants and participating and non-participating GP practices and iii) to describe attrition rates in the follow-up cohort.

6.3 **Methodology**

6.3.i Design

The baseline data from the SOUL-D study, a prospective cohort with newly diagnosed (<6 months) type 2 diabetes, were used.

Assessment of GP participation

All GP practices in Lambeth, Southwark and Lewisham were invited to take part in the study (details of this process are described in Chapter 5).

Data on the characteristics of GP surgeries were collected in order to compare those who chose to participate with those who did not. GPs were compared on the following characteristics: i) borough (Lambeth, Southwark or Lewisham), ii) patient list size, iii) percentage of patients with type 2 diabetes, iv) number of doctors, v) number of

nurses, vi) services and clinics (defined as a temporal allocation of healthcare resources primarily devoted to a specific condition for example, asthma clinic), vii) diabetes services (defined as a temporal allocation of healthcare resources primarily devoted to the treatment of diabetes), viii) IMD (described in Chapter 5; using the postcode of the GP instead of the participant).

Data for patient list sizes and numbers of patients with diabetes were obtained retrospectively from the QOF for April 2010 – March 2011 (Health and Social Care Information Centre) (HSCIC 2011). Data on the numbers of doctors and services and clinics were obtained from the NHS choices website in which was last updated between June 2012 and November 2013 by Lambeth, Southwark and Lewisham Clinical Commissioning Groups (http://www.nhs.uk/service-search).

Assessment of patient participation

The age, gender and ethnicity (where data were available) of all individuals invited to take part in SOUL-D were recorded on standardized eligibility forms (Appendix II).

Demographic variables at baseline

Details of variables are described in Chapter 5. Baseline data were collected by trained research assistants using standardised data collection schedules. Demographic variables were: age, gender, ethnicity, employment status, socio-economic status (NS-SEC), educational attainment and English as a second language.

Biological variables at baseline

Biological data were collected by standardised clinical assessment, from medical records or from venous blood samples which were drawn following an overnight fast (no food or drink other than water) for a minimum of 8 hours. Biological variables at baseline were: BMI, waist circumference, blood pressure, data on previous macrovascular event or microvascular complications, diabetes medication, HbA1c (mmol/mol) and total cholesterol: high density lipoprotein cholesterol ratio (TC:HDL ratio) as a measure of serum lipid profile. Mortality data were also collected for deceased participants. Death certificates were obtained and primary cause of death recorded. Cause of death was categorised into i) cancer, ii) infection, iii) cardiovascular or iv) not known, where data were unobtainable.

Psychological variables

Data were collected using a self-report questionnaire. Depression was assessed using the Patient Health Questionnaire – 9 (PHQ-9) (Spitzer et al. 1999). A score of ≥ 10 represents the likelihood of depression.

6.3.ii Statistical Analyses

Data were inputted and statistical analyses conducted using IBM SPSS Statistics 20 (IBM SPSS Inc, Chicago, IL, USA).

Data were checked for normality. Descriptive data were summarised as mean (standard deviation) or frequency (percentage). For HbA1c, data were skewed and the median (IQR) was reported in descriptive analyses.

For comparisons of participating GP surgeries, participant attrition and presence of outcome data, chi squared was used for categorical variables and t-tests or ANOVA were used for continuous variables. LnHbA1c was used in analyses, but untransformed median (IQR) are reported in tables. Bonferroni's post hoc comparisons were used to test for differences between categories.

6.4 **Results**

6.4.iii Characteristics of GP participation

Out of 138 GP surgeries across the London boroughs of Lambeth (n = 48), Southwark (n = 42) and Lewisham (n = 43), 96 (70%) agreed to participate. Data are incomplete for 4 practices (1 participated, 3 did not participate), because they have since closed down. Table 7 shows the characteristics of participating and non-participating GP practices which were all offered financial incentives from service support costs (via NIHR Comprehensive Research Network) to take part in SOUL-D. Significantly more practices in Southwark declined to take part in the study (45.2%) when compared to Lambeth (18.8%) and Lewisham (20.9%). Practices not participating in SOUL-D also had significantly smaller patient list sizes (3376 vs 4106 registered patients) and fewer doctors (3.7 vs 5.4 doctors). There were no significant differences in the numbers of nurses, number of patients with diabetes, in the provision of services and clinics, diabetes services or in deprivation scores of the practice.

Table 7 Characteristics of participating and non-participating GP surgeries in the SOUL-D study

	Participating GPs (n = 96)	**Non-participating GPs (n = 38)**	**p value**
Borough			0.01
Lambeth	39 (81.3%)	9(18.8%)	
Lewisham	34 (79.1%)	9 (20.9%)	
Southwark	23 (54.8%)	19 (45.2%)*	
Mean patient list size (n)	7648 (4106.9)	5823 (3376.9)	0.02
Patients with diabetes (%)	4.0 (1.20)	3.9 (1.20)	0.80
Mean number of doctors	5.4 (2.89)	3.7(2.39)	0.003*
Mean number of nurses	1.8 (1.74)	1.2 (1.30)	0.09
Mean number of specialist services	4.3 (3.94)	3.4 (3.47)	0.21
Provides a diabetes specialist service	7 (7.5%)	1 (3.0%)	0.36
IMD			0.83
1st Quintile (most deprived)	45 (46.9%)	19 (51.4%)	
2nd Quintile	40 (41.7%)	14 (37.8%)	
3rd Quintile	8 (8.3%)	3 (8.1%)	
4th Quintile	1 (1.0%)	1 (2.7%)	
5th Quintile (least deprived)	2 (2.1%)	0 (0.0%)	

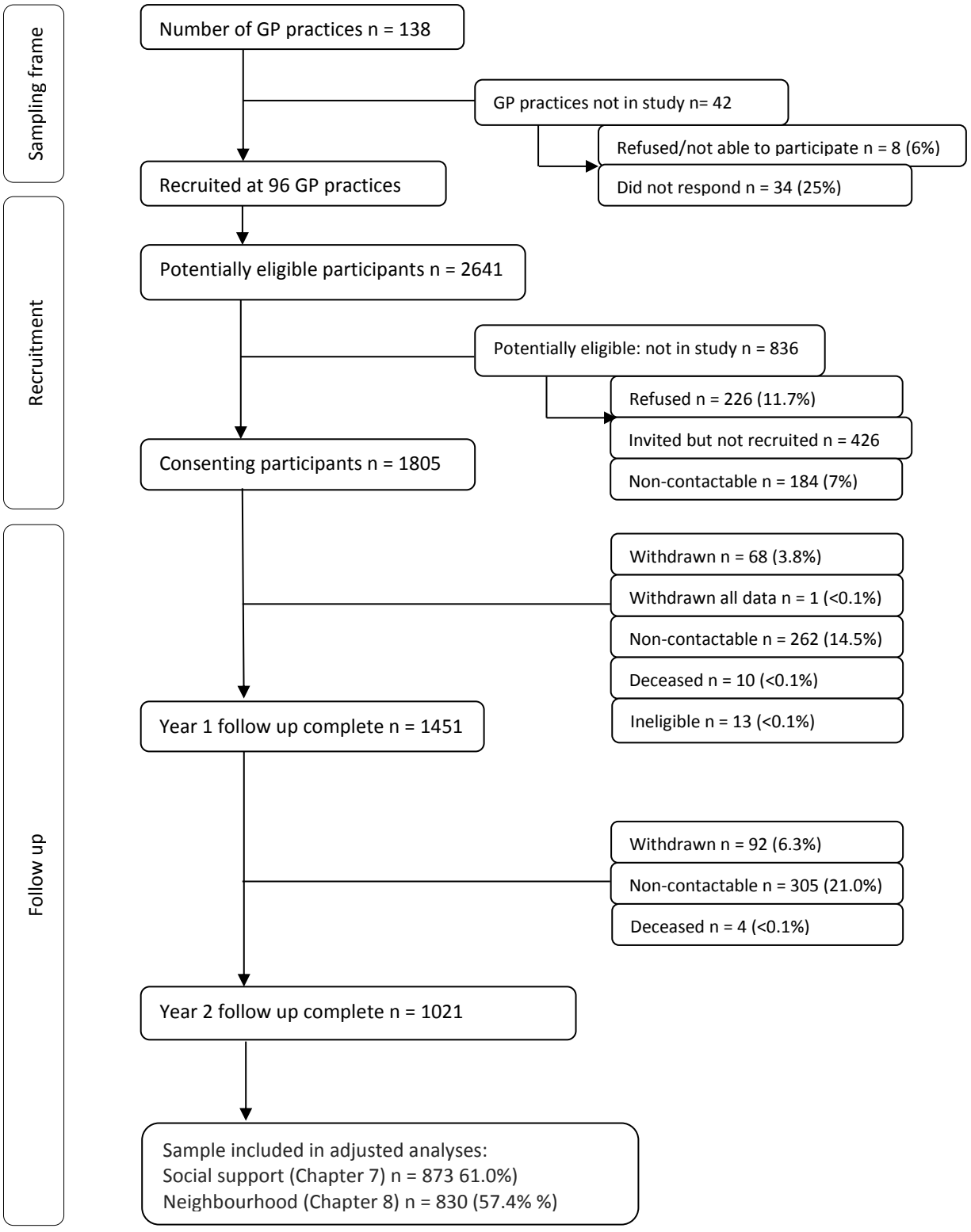
Data are presented as mean (standard deviation) for continuous variables or n(%) for categorical variables; To statistically test for differences in surgery participation, chi squared was used for categorical variables and t tests were used for continuous variables; *Denotes the cell contributing to significance in chi squared test; IMD: Index of Multiple Deprivation (based on surgery postcode).

6.4.iv Characteristics of patient participation vs non participation

All individuals with a recent diagnosis (< 6 months duration) at participating GP practices were invited to participate. There were 2641 potentially eligible patients with newly diagnosed type 2 diabetes identified from 96 GP practices between September 2008 and September 2013. From this 1805 individuals were recruited. Only participants who consented to participate in SOUL-D between September 2008 and November 2011 were included in this thesis (n = 1447). There were 14 participants who were found to be ineligible and 1 participant who withdrew consent following entry to the study. These participants are removed from subsequent analyses. The total sample included in analyses is 1432.

Figure 17 describes the SOUL-D study flow chart. When compared to participants, non-participants were younger (52.3 (±11.60) v 56 years (±11.07) p < 0.001) and more likely to be male (62.8% v 54.8%, p = 0.01). Ethnicity data were available for 11.7% of non-

participants; 50% were white, 16% were black and 34% were of South Asian/ other ethnicity. Data on additional demographic characteristics could not be obtained because SOUL-D did not have ethical approval for further data collection.



*missing (n = 20).

Figure 17 The SOUL-D study flow chart (only participants who had finished their year 2 follow-up by November 2013 were included in this thesis n = 1432)

6.4.v Demographic and clinical baseline characteristics of the sample

The main demographic and clinical characteristics of the sample can be found in Table 8. The mean age was 56 years (±11.06); 55% were male; and 51%, 38% and 11% of the sample were white, black and south Asian/ other ethnicities respectively.

Just under half (47.4%) the cohort were in full- or part-time employment and 27% were retired. The majority (56.1%) of the cohort were married or cohabiting, 14% were separated or divorced, 6% were widowed and 25% single. Most participants (35.5%) were in managerial, administrative or professional occupations, however a considerable proportion (22%) were in semi-routine and routine occupations. One quarter of participants (22.3%) did not have any formal educational qualifications and there were 260 (18.2%) participants for whom English was their second language.

The mean duration of diabetes was 4.8 months (±2.11). The mean BMI was in the obese range (31.9 kg/m^2 (± 6.50)), the median HbA1c was 48.6 mmol/mol (IQR = 43.17 – 48.63) and TC:HDL ratio was 4.1 (±1.29). The mean systolic and diastolic blood pressure for the sample was 136.0 mmHg (±17.82) / 83.1 mmHg (±10.80) respectively. Just over half (53.9%) of participants were taking oral antidiabetic drugs or insulin for their diabetes. In the cohort, 9% had a history of a macrovascular event and 28% had a history of microvascular complications. There were 281 (14.6%) participants who scored positive for depression caseness using the PHQ-9 and almost 20% of the sample were smokers.

Table 8 The baseline demographic and clinical characteristics of the cohort (n=1432)

Variables		Total n	Mean (SD) / n (%)
Age (years)		1432	56 (11.06)
Gender			
	Female	1432	647 (45.2%)
	Male		785 (54.8%)
Ethnicity		1432	
	White		725 (50.6%)
	Black		546 (38.1%)
	South Asian/other		161 (11.2%)
Employment status		1432	
	Employed		686 (47.4%)
	Unemployed		361 (25.2%)
	Retired		385 (26.9%)
Marital status			
	Married / cohabiting	1432	804 (56.1%)
	Separated / divorced		196 (13.7%)
	Widowed		79 (5.5%)
	Single		353 (24.5%)
NS-SEC		1329	
	Managerial administrative or professional occupations		508 (35.5%)
	Intermediate occupations		140 (9.8%)
	Small employers and own account workers		165 (11.5%)
	Lower supervisory and technical occupations		200 (14.0%)
	Semi-routine and routine occupations		316 (22.1%)
Educational attainment		1008	
	Higher degree or above		208 (14.5%)
	Advanced Level		285 (19.9%)
	Up to GCSE level		196 (13.7%)
	No qualifications		319 (22.3%)
English as 2nd language		977	
	Yes		260 (18.2%)
	No		717 (50.1%)
Duration of diabetes (months)		1426	4.8 (2.11)
Microvascular complications		1045	
	Yes		404 (28.2%)
	No		641 (44.8%)
Macrovascular complications		1408	
	Yes		132 (9.2%)
	No		1276 (89.1%)
Antidiabetic medication			
	Yes	1410	772 (53.9%)
	No		638 (44.6%)
Smoking status		1372	
	Yes		281 (19.6%)
	No		1091 (76.2%)
Depression status		1413	
	Yes		211 (14.6%)
	No		1202 (83.1%)
HbA1c (mmol/mol)		1330	48.6 (43.17 – 48.63)[a]
BMI (kg/m^2)		1429	31.9 (6.50)
Total cholesterol: HDL ratio		1244	4.1 (1.29)
Systolic BP (mm Hg)		1372	136.0 (17.82)
Diastolic BP (mm Hg)		1372	83.1 (10.80)

Data are presented as mean (SD) for continuous variables and n (%) for categorical variables; n: number in sample for which data is recorded as some were missing; [a] data are median (interquartile range); NS-SEC: National statistics socio-economic classification; BMI: body mass index; HDL: high density lipoprotein; BP: blood pressure.

6.4.vi Recruitment results

The aim was to recruit a cohort with newly diagnosed type 2 diabetes representative of the residents of an inner city, multi-ethnic population. Table 9 describes the demographic characteristics of the study setting (individuals with and without diabetes in Lambeth, Southwark and Lewisham) compared to the recruited cohort. On average, 36% of the population of Lambeth, Southwark and Lewisham is from black or ethnic minority groups. In the SOUL-D cohort, 49% of the sample was of black, South Asian or other ethnic origin. This indicates an over-recruitment of black and South Asian participants in the SOUL-D study. In the SOUL-D cohort, levels of employment are comparable to the local population but significantly more individuals had no formal qualification (22.3% vs ~ 9%).

Table 9 Demographic data of the sampling frame compared to the recruited cohort

	Lambeth	**Southwark**	**Lewisham**	**SOUL-D**
Population	303,100	288,300	275,900	1432
BME population (%)	38	37	34	49.3
Employment* (%)	71.9	69.8	68.3	65.5
No qualifications (%)	10.2	9.5	7.3	22.3

BME: Black and minority ethnic; *% of working age population; Data obtained from Annual Population Survey (Office of National Statistics 2013)

6.4.vii Attrition at 2 years follow-up

Of 1432 participants, 1021 (71.3%) were followed-up at year 2; 343 participants could not be contacted, 92 had withdrawn and 14 had died. Data were collected at year 2, with consent, from medical records of 100 participants lost to follow-up. At year 2 there is outcome data for 78.3% participants.

There were significant differences in demographic characteristics between those who were followed-up and those who were lost to follow-up (Table 10). Participants who were lost to follow-up were significantly younger, more likely to be female, of black

ethnicity, less likely to be retired, depressed and have a higher HbA1c than those who were followed-up at 2 years.

Table 10 The baseline characteristics of participants in SOUL-D who were followed-up versus those lost to follow-up at 2 years (n = 1432)

	Followed-up (n = 1021)	**Lost to follow-up (n = 411)**	**p value**
Age (years)	57.0 (10.71)	53.4 (11.51)	< 0.001
Gender			
Males	580 (56.8%)	205 (49.9%)	0.02
Females	441 (43.2%)	206 (50.1%)*	
Ethnicity			< 0.001
White	556 (54.5%)*	169 (41.1%)	
Black	356 (34.9%)	190 (46.2%)*	
South Asian/other	109 (10.7%)	52 (12.7%)	
Employment status			0.01
Employed	475 (46.5%)	211 (51.3%)	
Unemployed	247 (24.2%)	114 (27.7%)	
Retired	299 (29.3%)	86 (20.9%)*	
Marital status			0.52
Married / cohabiting	567 (55.5%)	237 (57.7%)	
Separated / divorced	141 (13.8%)	55 (13.4%)	
Widowed	62 (6.1%)	17 (4.1%)	
Single	251 (24.6%)	102 (24.8%)	
Depressed			0.03
Yes	138 (13.7%)	73 (18.1%)*	
No	872 (86.3%)	330 (81.9%)	
HbA1c (mmol/mol)	51.8 (12.81)	55.1 (16.71)	0.03

Data are presented as mean (standard deviation) for continuous variables or n(%) for categorical variables.
To test for differences in status at year 2, Chi squared was used for categorical variables and ANOVA was used for continuous variables. *Denotes the cell contributing to significance in Chi Squared test.

Table 11 describes the characteristics of non-contactable, withdrawn and deceased participants. Non contactable participants were significantly younger and less likely to be retired, participants who withdrew were more likely to be of white ethnicity and retired and participants who had died were less likely to be of black ethnicity and in employment.

Table 11 The characteristics of participants who were non-contactable, withdrawn or deceased at 2 years

	Non contactable (n = 305)	Withdrawn (n =92)	Deceased (n = 14)	p value
Age (years)	51.6 (10.79)	58.1 (12.23)	62.1 (9.96)	< 0.001
Gender				
Males	156 (51.1%)	39 (42.4%)	10 (71.4%)	0.09
Females	149 (48.9%)	53(57.6%)*	4 (28.6%)	
Ethnicity				0.001
White	108 (35.4%)	51 (55.4%)*	10 (71.4%)	
Black	158 (51.8%)	30 (32.6%)*	2 (14.3%)*	
South Asian/other	39 (12.8%)	11 (12.0%)	2 (14.3%)	
Employment status				< 0.001
Employed	175 (57.4%)	35 (38.0%)	1 (7.1%)*	
Unemployed	88 (28.9%)	22 (23.9%)	4 (28.6%)	
Retired	42 (13.8%)*	35 (38.0%)*	9 (64.3%)*	
Marital status				0.39
Married / cohabiting	166 (54.4%)	62 (67.4%)	9 (64.3%)	
Separated / divorced	45 (14.8%)	9 (9.8%)	1 (7.1)	
Widowed	12 (3.9%)	4 (4.3%)	1 (7.1%)	
Single	82 (26.9%)	17 (18.5%)	3 (21.4%)	
Depressed				0.22
Yes	53 (17.7%)	15 (16.9%)	5 (35.7%)	
No	247 (82.3%)	74 (81.3%)	9 (64.3%)	
HbA1c (mmol/mol)	50.8 (20.49)	47.5 (15.30)	54.1 (31.69)	0.16

Data are presented as mean (standard deviation) for continuous variables or n(%) for categorical variables;
To test for differences at year 2, chi squared was used for categorical variables and ANOVA was used for continuous variables; *Denotes the cell contributing to significance in chi squared test.

Although reasons for a participant being non contactable were not individually recorded, there were 2 categories: i) those who could not be interviewed but did not want to withdraw: this group included individuals who were working, ill, carers or too busy and ii) those where no contact could be made: no response to multiple contact attempts, dead phone lines, those who had left the country for an extended period or had moved abroad, those who had moved surgery and not re-registered. For withdrawn individuals, contact had been made but they specified that they no longer wished to take part in the study.

At 2 years, 14 (1%) individuals had died. The primary causes of death are listed in Table 12.

Table 12 Primary causes of death in the SOUL-D cohort at 2 years follow-up

Cause of death	**Frequency (%) (n = 14)**
Cancer	5 (35.7%)
Infection	3 (21.4%)
Cardiovascular disease	4 (28.6%)
Not known	2 (14.3%)

6.4.viii Participants without outcome data at year 2

Table 13 compares the demographic characteristics of participants with an HbA1c value (the primary outcome) at year 2 with those missing outcome data. Data were missing where study bloods had not been completed and no record of HbA1c could be obtained from medical records. Individuals missing HbA1c were significantly younger than those with HbA1c at year 2 (57 (±10.89) vs 44 years (±11.34)). They were significantly more likely to be black and in full- or part-time employment. There were no significant differences in gender, marital status, depression status or BMI.

Table 13 The demographic characteristics of individuals with outcome data (HbA1c) at year 2 compared to those without outcome data

Variables		Outcome data (n = 1024)	No outcome data (n = 405)	p value
Age (years)		56.6 (10.89)	54.5 (11.34)	0.001
Gender				0.10
	Female	449 (69.5%)	197 (30.5%)	
	Male	575 (73.4%)	208 (26.6%)	
Ethnicity				0.01
	White	546 (75.3%)	179 (24.7%)	
	Black	368 (67.4%)	178 (32.6%)*	
	South Asian/other	113 (70.2%)	48 (29.8%)	
Employment status				0.03
	Employed	485 (70.7%)	201 (29.3%)*	
	Unemployed	247 (68.4%)	114 (31.6%)	
	Retired	295 (76.6%)	90 (23.4%)	
Marital status				0.29
	Married / cohabiting	565 (70.3%)	239 (29.8%)	
	Separated / divorced	147 (75.0%)	49 (25.0%)	
	Widowed	62 (78.5%)	17 (21.5%)	
	Single	253 (71.7%)	100 (28.3%)	
Depression status				0.37
	Yes	146 (69.2%)	65 (30.8%)	
	No	868 (72.2%)	334 (27.8%)	
BMI (kg/m^2)		31.9 (6.42)	31.9 (6.70)	0.91

Data are presented as mean (standard deviation) for continuous variables or n(%) for categorical variables; To test for differences between those with and those without outcome data, chi squared was used for categorical variables and t tests were used for continuous variables; *Denotes the cell contributing to significance in chi squared test; Data for educational attainment and English as a second language is not available for these participants as this data is collected at year 2.

6.4.ix Comparison of the SOUL-D study to other newly diagnosed type 2 diabetes cohorts

Table 14 describes baseline data from the SOUL-D study with other cohorts of newly diagnosed type 2 diabetes. There are no statistical tests as they are not from the same study population. Interpretations of descriptive comparisons across datasets must be made with caution due to differences in eligibility criteria and methods of data collection. The largest cohort, the landmark UKPDS recruited over 20 years ago between 1977 and 1991. Compared to SOUL-D, the mean age of the sample was lower (53 vs 56 years), the median HbA1c was significantly higher (76.0 vs 48.6 mmol/mol) but BMI was lower (27.5 vs 32.3 kg/m^2). The systolic and diastolic blood pressures were equivalent (134/82 vs 135/82 mmHg). The South of England Study, recruited slightly later between 1994 and 1995, reported a mean BMI of 30.7 kg/m^2, higher than the UKPDS and more comparable to SOUL-D. HbA1c data were not available from this

study. In a large retrospective study of medical records between 1996 and 1998, Hillier and colleagues report a mean HbA1c of 58.5 mmol/mol and the highest mean BMI of all the studies (33.3 kg/m^2). This study was conducted in the USA and only included individuals with health insurance records and may therefore not be representative of the local population. The Poole Study, a single site incidence study, reports a mean age of 64 years, the oldest of all the studies. The mean HbA1c was also the highest (94.5 mmol/mol) but the mean BMI (31.5 kg/m^2) was lower than in the SOUL-D study. In the more recent DESMOND cohort (2004-2005), the mean HbA1c was significantly higher (65.0 vs 48.6 mmol/mol). More contemporary cohorts, the ADDITION Europe and the Early Activity In Diabetes (Early ACTID) trial, report similar HbA1c (48.6 vs 49.4 vs 48.6 mmol/mol respectively) and mean BMIs to SOUL-D (31.6 vs 31.5 vs 31.9 kg/m^2 respectively), all significantly higher than UKPDS. A significant difference between all the studies and SOUL-D is the ethnic diversity: 51% of SOUL-D was white compared to between 86% and 96% in other cohorts.

Table 14 Baseline demographic and biomedical data from studies of newly diagnosed type 2 diabetes (adapted from Khunti et al. 2008)

	UKPDS[1]	**South of England Study**[2]	**Hillier et al.**[3]	**Poole Study**[4]	**DESMOND**[5]	**ADDITION-Europe**[6]	**ACTID**[7]	**SOUL-D***[8]
Location	Multi-site, UK	Single site, England	Single site, USA	Single site, England	Multi-site, UK	Multi-site, Denmark, Netherlands, UK	Single site, England	Single site, England
Study design	RCT, new cases diagnosed at practice level (15 centres).	RCT, new cases diagnosed at practice level (15 practices).	Retrospective study. Data from health insurance records.	Incidence study, new cases diagnosed at practice level (15 practices).	RCT, new cases diagnosed at practice level (162 practices).	RCT, new cases diagnosed at practice level (343 practices).	RCT, new cases diagnosed at practice level (217 practices).	Population cohort, new cases diagnosed at practice level (96 practices).
Recruitment period	1977-1991	1994-1995	1996-1998	1996-1998	2004-2005	2001-2006	2005-2008	2008-2013
Age eligibility (years)	25-65	40-64	45-70	All new cases	>18	40-69	30-80	18-75
N	5102	197	2160	706	824	3057	593	1805
% male	59	57.9	56	54	55	58.5	65.2$^{\mu}$	54.8
Mean age	53$^{\wedge}$	55.8±6.8	-	64.3±13.2	59.5±12.1	60·3 ± 6·9	59.8 ± 10.0 $^{\mu}$	56.0 ±11.1
% white	86	-	-	'mainly white'	97$^{\Omega}$	93-96	96	51
HbA1c (mmol/mol)	76.0$^{\wedge}$	-	58.5	94.5	56.3 (47.5–79.2)$^{\wedge}$	48.6 (43.2–56.3)$^{\wedge}$	49.4 ± 10.6 $^{\mu}$	48.6 (15.30)$^{\wedge}$
BMI (kg/m^2)	28$^{\wedge}$	30.7±5.8	33.3±27	31.5±7.0°	32.4±6.2	31.6±5.6	31.5 ± 5.6 $^{\mu}$	31.9 (6.50)
SBP	143 $^{\varepsilon}$	144 (80-190)‡	135±17	142±21°	141±18	148.5 (22.1)‡	-	136.0 (17.82)
DBP	87 $^{\varepsilon}$	86 (60-118)‡	79±10	81±12°	82±11	86.1 (11.1)‡	-	83.1 (10.80)

[1]:UKPDS (1991); [2]: Griffin et al. (2000); [3]: Hillier and Pedula (2001); [4]: Gatling et al. (2001); [5]: Khunti et al. (2008); [6] : Griffin et al. (2011); [7] : Andrews et al. (2011). Data are presented as mean (SD) unless otherwise specified. BMI: Body mass index; SBP: Systolic blood pressure; DBP Diastolic blood pressure; - : data not available; *Demographic and biomedical data are from the first 1432 participants of SOUL-D; ^: median (IQR); ‡: Mean from intervention arm, which did not differ from control arm; $^{\Omega}$: ,percentage of white males which did not significantly differ from females (96%); °: Data from subgroup (*n* = 428) aged 35–74 years and free of existing cardiovascular symptoms; $^{\mu}$: Data from subgroup (n = 527); ε: n = 2906.

6.5 **Discussion**

This chapter presented the characteristics of a cohort immediately after the diagnosis of type 2 diabetes in a multi-ethnic, inner city setting and compared these to existing cohorts. It describes the representativeness of the sample at a GP and individual level, and described participant attrition at 2 years follow-up.

There have been few large studies of newly diagnosed type 2 diabetes. The largest study for comparison is the landmark UKPDS which recruited over 20 years ago (UKPDS 1991) and to which the clinical characteristics of SOUL-D are notably different. The lower mean age in UKPDS may reflect study inclusion criteria where individuals over 65 years were not eligible, but in SOUL-D, HbA1c was significantly lower and the majority of individuals were diagnosed by opportunistic screening with no symptoms (Winkley et al. 2013). Participants in SOUL-D had a higher mean BMI but systolic and diastolic blood pressures were equivalent. The clinical characteristics of more recent studies, DESMOND, ADDITION – Europe and ACTID are more similar. Although in DESMOND the mean HbA1c was significantly higher. The mean BMIs are comparable and higher than UKPDS. Also notable are the ethnic differences. In SOUL-D, 51% were white, compared to 86% in UKPDS. More recent studies also reported a white population of 93 - 97%. Ethnic differences may therefore contribute to some of the differences between SOUL-D and other cohorts. Other reasons for differences between these cohorts are i) changes in screening and clinical management in primary care, leading to proactive case finding and higher and earlier detection rates of type 2 diabetes; ii) a rise in prevalence of obesity over the past 20 years and iii) the increased risk of type 2 diabetes in ethnic minority groups.

Another important finding in the SOUL-D cohort was the lower than expected prevalence of depression. Based on self-report questionnaires, previous research reports a prevalence of 26%, larger than the 14% in our sample (Anderson et al. 2001).

However, this may be explained by the newly diagnosed nature of our sample as the risk of depression increases with diabetes complications, disability and mortality.

Significant efforts were made to ensure that the recruited population were representative. Selection bias by ethnicity is unlikely to be a major concern, however younger individuals and males were less likely to participate in SOUL-D. When compared to the local population (individuals with diabetes and those without), black and South Asian / other ethnicities were over represented in SOUL-D, fewer individuals were in employment and significantly more had no qualifications. These findings may highlight the demographic characteristics of individuals being diagnosed with type 2 diabetes and reflect two established associations: i) the increased risk of type 2 diabetes in black and South Asian ethnicities (Barroso 2005) and ii) the increased risk in individuals from lower socio-economic status (Evans, Newton et al. 2002) (employment and educational attainment are often used as proxies for socio-economic status). The enhanced proportion of black and South Asian people in SOUL-D may also reflect a willingness of this population to engage in research, addressing a misperception in the research world.

At a GP level, there were few differences between participating and non-participating GP practices. Those recruited were largely representative of the local boroughs. Significantly more practices in Southwark did not participate in the study. This may be a result of organisational differences between Clinical Commissioning Groups (CCG). Additionally, this borough may be less familiar with research and therefore not as willing to participate as Lambeth or Lewisham. However differences predominantly related to the capacity of GP practices, for example list sizes and number of doctors. Smaller practices (fewer registered patients and doctors) may find it more difficult to accommodate large research studies than larger practices and the perceived time burden may also be a limiting factor. This has previously been highlighted as a major constraint to research participation in primary care (Jones 2012). However, given the

large and inclusive sampling frame the findings in this thesis are likely to be generalisable to individuals with newly diagnosed type 2 diabetes in the UK.

The characteristics of participants who were not followed-up at year 2 and who did not have outcome data at year 2 may reflect the working population who may have had less time to attend appointments or who may be more difficult to contact during working hours. These findings are similar to previous data which describe mental health, cumbersome protocols, time and low socio-economic status as barriers to study participation and retention (Yancey et al. 2006). Alternatively, individuals lost to follow-up in SOUL-D may have been proactive in their yearly diabetes checks at the GP and unwilling to attend additional appointments.

Limitations of the recruitment strategy of SOUL-D are that it sampled an area that may not reflect the ethnic and socio-economic make-up of the UK. However, it is important from a public health perspective; an area with a disproportionate burden of type 2 diabetes and therefore healthcare expenditure and an area representative of many large European and North American cities. The strengths in the design and recruitment of SOUL-D are i) the high participation rate (only 32% of invited individuals did not take part in the study); ii) the high representation of individuals of black ethnicity as this demographic group has not been previously described in a newly diagnosed sample and iii) the comprehensive recruitment of GP practices across the 3 boroughs of South East London (only 6% declined to take part in the study and 25% did not respond). This suggests that if resources had allowed researchers to dedicate more time to practice recruitment, even more may have participated.

6.6 **Conclusion**

This chapter described the baseline characteristics of a representative inner-city cohort with newly diagnosed type 2 diabetes. The results suggest that the demographic

profile of newly diagnosed type 2 diabetes may be changing. Compared to the landmark UKPDS, at diagnoses, patients have lower HbA1c but higher BMI, reflecting changes in clinical practice and the increasing prevalence of obesity. The profile of SOUL-D is similar to the recent DESMOND, ADDITION-Europe and ACTID cohorts. The overrepresentation of individuals of black and South Asian ethnicity in SOUL-D, when compared to the local area, reflects the increasing prevalence of type 2 diabetes in these groups and indicates that people from all ethnic groups are willing to participate in research. These findings may inform resource allocation within primary and secondary disease prevention.

The next chapter reports the prospective association between social support at baseline and glycaemic control at 2 years.

Chapter 7 Social support and glycaemic control: a prospective analysis

7.1 **Synopsis**

The aim of this chapter is to investigate the association between social support and glycaemic control at 2 years post diagnosis in individuals with type 2 diabetes.

Social support is associated with worse biomedical outcomes, morbidity and mortality, but there are few prospective studies investigating the association between social support and glycaemic control in type 2 diabetes. A prospective cohort with newly diagnosed type 2 diabetes was recruited from primary care in three adjacent boroughs of South East London. Social support variables were collected at baseline; structural social support was measured using: i) marital status ii) social network size and iii) community ties and functional support was measured using perceived social support. The main outcome was glycaemic control (HbA1c (mmol/mol)) at 2 years. From 96 GP surgeries, 1432 individuals with newly diagnosed type 2 diabetes were recruited. In mixed-effects multi-level regression analyses, controlling for relevant confounding and for the possible clustering effect of GPs, there was no significant association between social support variables and HbA1c at 2 years follow-up after accounting for multiple testing. The association between social support and HbA1c at 2 years did not differ across demographic group. However, there were some statistical trends and these are presented. These analyses provide tentative evidence to suggest that the beneficial effect of social support observed in the general population may not directly translate to individuals with type 2 diabetes. Possible explanations for these findings are discussed.

7.2 **Introduction**

Summarising the literature reviews in chapters 2 and 3, the key findings are as follows:

Social support is an important explanatory variable with prognostic significance for health outcomes. Epidemiological research reports an inverse association between social support and morbidity and mortality (Berkman et al. 2000) and its effects on health may be comparable to established risk factors such as smoking, obesity and physical activity (Holt-Lunstad et al. 2010).

Social support is a multifaceted construct consisting of structural and functional dimensions (Lin et al. 1999) which may influence health directly, by assisting with self-care behaviours, or indirectly, where social support 'buffers' the potentially harmful effects of acute or chronic stressors (Cohen and Wills 1985). Despite positive connotations, certain forms of social support may be unwanted or misinterpreted as nagging or harassment and impact negatively on health (Clark and Nothwehr 1997, Mayberry and Osborn 2012).

In type 2 diabetes, the social context of an individual may be an important supportive resource. The management of the disease is largely the responsibility of the individual. The support of a spouse or partner, family members or extended social networks (informal support) may be valuable when adjusting to the diagnosis, making lifestyle changes, adherence and coping with diabetes complications and disability. Formal (support from health care professionals) and informal social support have been associated with improved diabetes self-management (Tang et al. 2008, Wing et al. 1991, Trento et al. 2001) and adherence to prescribed therapies in RCTs and observational studies (Glasgow and Toobert 1988, Mayberry and Osborn 2012) but a systematic review found only five intervention studies and reported a beneficial effect of social support (group visits to the clinician) in 20% (Trento et al. 2001, van Dam et al.

2005). Furthermore, our own recent systematic review only found tentative evidence of an association between informal social support and glycaemic control in observational studies (Stopford et al. 2013) although this was probably due to marked variation in study populations, setting, measurement of social support and definition of HbA1c (Chapter 3).

The receipt, provision and utilisation of social support may differ by demographic group. Most widely reported are gender variations in social support (Umberson 1992), but differences may also exist between ethnic group or according to depression status. Using these factors as covariates in analyses may mask associations between social support and health outcomes.

The increasing economic burden of type 2 diabetes and pressures placed on healthcare systems necessitate the identification of non-pharmacological, readily available and cheaper potentially modifiable targets of intervention. Informal social support may be one such target. In a society where tailored interventions are becoming a necessity, support from family and friends is a ready-made, ready-to-use and bespoke intervention which, surprisingly, has not been fully utilised in individuals with type 2 diabetes. Furthermore, few epidemiological studies have even aimed to identify the essential and 'active' components of social support in type 2 diabetes. Whether the beneficial effect of social support translates to type 2 diabetes needs to be tested before mechanisms can be investigated and tailored interventions developed.

Aims:

The aims of this chapter are to assess: i) whether structural (marital status, social network and community ties) and functional (perceived) support are associated with HbA1c at 2 years, and ii) to investigate whether the association between social support and HbA1c is modified by gender, ethnicity and depression status.

Hypotheses:

1. Increased structural social support will be associated with lower HbA1c at 2 years.
2. High levels of perceived social support will be associated with lower HbA1c at 2 years.
3. The association between social support and HbA1c at 2 years will be stronger in i) males, ii) those from ethnic minority groups and iii) individuals who are not depressed.

7.3 **Methodology**

7.3.i Design

This study is embedded within the SOUL-D study, a prospective cohort with 2 years follow-up.

7.3.ii Setting and sample

As described in detail in Chapter 5, this is a population based multi-ethnic and socio-economically diverse cohort with newly diagnosed type 2 diabetes in 3 inner-city boroughs of South East London.

7.3.iii Explanatory variables

In this section, the social support measures are briefly outlined. A full description of measures can be found in Chapter 5. The rationales for variables used as confounders in analyses are described.

Social Support

Structural social support

i) Marital status. Participants reported whether they were i) married or cohabiting; ii) separated or divorced; iii) widowed or iv) single.

ii) Social network. Participants reported their weekly contacts, by type, in a typical week (Lin et al. 1999). Responses ranged from 0 – 10 weekly contacts.

iii) Community ties. Participants reported their participation in community activities across seven domains: faith related groups, job related associations, recreational groups, fraternal services, civic and political groups and senior citizen groups or other (Lin et al. 1999).

Functional social support

i) Perceived social support. Participants were asked whether they would be able to receive help or assistance on a regular basis (at least 2-3 times a week) should they need it, in 5 standardised hypothetical situations (Lin et al. 1999). Responses were: 1 = no, 2 = yes with difficulty or 3 = yes.

These social variables were chosen as they represent a comprehensive examination of the multifaceted nature of structural and functional social support.

7.3.iv Potential confounders

Age (years). The presence, type of, and need for social support changes across the life course. Increasing age has been associated with fewer and less frequently seen social contacts and less proximal networks (Ajrouch et al. 2001). As people get older, they are significantly disadvantaged in maintaining and strengthening social ties due to retirement, disability or death of a spouse or friends. Older individuals may increasingly rely on a small number of contacts – adult children for example, who may also have competing demands on their time. Although the size of social networks decrease the quality of each social relationship may increase. Importantly, diminishing social support is associated with poor self-care and adherence to medical regimen. This loss of social support is particularly pertinent to the older population who may be increasingly reliant on support and guidance in the day-to-day management of type 2 diabetes.

Gender. The receipt, provision and utilisation of social support varies across social groups, and variations between males and females are most frequently reported. Females report larger social networks with closer confiding ties. They may be more emotionally affected by their social networks, which may become a source of stress rather than support. Conversely, males report smaller social networks which serve a social purpose (as opposed to the confiding function observed in the social networks of females) and their spouse as their closest emotional contact (Shye et al. 1995). Social support is thought to exert a greater protective influence on morbidity and mortality in males (House et al. 1988) and this benefit is particularly evident in marriage (Umberson 1992). Females appear to provide more support to their spouses in ill

health (Neff and Karney 2005) but the support provided by husbands does not appear to vary according to problem severity.

Self-reported ethnicity: white, black or South Asian/other. The size of social networks and levels of available social support vary between ethnic groups, although inconsistencies in the literature make drawing conclusions difficult (Vaux 1985, Pollard et al. 2003). Certain ethnicities place a greater emphasis on two key social institutions: i) the family and ii) religious organisations. Strong family and religious ties are often more evident in ethnic minority groups and higher levels of satisfaction with support are reported, possibly because the majority of support is received from family members (Stopes-Roe and Cochrane 1990). However, the evidence is inconsistent. n the Whitehall II Study, South Asian participants reported lower levels of support and higher levels of negative support than white participants and white and black participants reported comparable levels of support (Hemingway et al. 2001), but in the Health Survey for England black individuals reported lower levels of social support (Shields and Price 2005). The increased emphasis placed on the importance of family in certain ethnicities notionally increases the likelihood of receiving support when needed. It is known that individuals from black and South Asian ethnicities display poorer glycaemic control and diabetes outcomes than their white counterparts so these ethnic variations in social support provision may hold important implications for the day-to-day management of type 2 diabetes.

Employment status: employed, unemployed or retired. In this chapter, employment status is utilised as a confounding variable for two reasons: i) to serve as a proxy for individual socio-economic status and ii) due to its effect on social networks and, consequently, the availability of support.

There is an established, and undisputed, association between low socio-economic status and adverse health. Perhaps due to this, there has been significantly less

research than may have been expected investigating the direct association between socio-economic status and specific outcomes in the last few decades. Socio-economic status is now treated as a key confounder in health research. As such, the search for additional aetiological risk factors is often regarded as flawed unless socio-economic status is controlled.

Employment may bring, or at least encourage, additional social benefits. People who are employed have more social contacts than individuals who are not working or retired. Being in employment provides more opportunities for social contact and subsequently social support. Employment provides a 'ready-made' social network with a shared sense of purpose and belonging. It should also be considered that those who are retired or unemployed may have stronger social ties with a smaller network. These individuals may have more time to invest in reciprocal relationships with each social contact and therefore the functionality or quality or these relationships may outweigh those formed in employment.

Depression status was measured using the Patient Health Questionnaire – 9 (PHQ-9) (Spitzer et al. 1999). A value ≥ 10 indicates the likelihood of depression. Depression severity is inversely associated with social support and depressed individuals report lower levels of social support than those who are not depressed (George et al. 1989). Furthermore, longitudinal evidence suggests that depressed individuals who have good levels of social support demonstrate rapid symptom improvement and lower risk of relapse (Alexopoulos et al. 1996). In diabetes, depression is associated with poor diabetes self-care and glycaemic control (Ciechanowski et al. 2000).

Diabetes medication: i) Yes: prescribed oral antidiabetic drugs or insulin or ii) No: not prescribed any diabetes medication. In a general medical setting, non-adherence is relatively high but support from social contacts may promote adherence. This may be particularly true for unintentional non-adherence (non-adherence due to cognitive

impairment, emotional stress or due to demands on an individual's time) but may be less evident in the case of intentional non-adherence (non-adherence due to unwanted side-effects, for example).Friends and family may promote adherence by offering practical assistance or psychological support, for example, improving self-esteem or buffering the stresses of being ill (DiMatteo 2004). For people with type 2 diabetes, polypharmacy is common and evidence suggests that Social support may be particularly helpful when medication regimen is complex (Gallant 2003)..

Previous macrovascular event was defined as a history of myocardial infarction, coronary artery bypass graft, cerebrovascular accident and carotid or limb revascularisation. This was self-reported and validated from medical records. Poor social support is consistently associated with the onset and progression of cardiovascular disease in cross-sectional and longitudinal studies (Uchino 2006). Small social networks, being single or widowed, have been independently associated with increased risk of coronary artery calcification (Kop et al. 2005) and cerebrovascular accident (Rutledge et al. 2008). From another perspective, individuals who have had a previous macrovascular event may have developed and established an optimally functioning social network. Thus, following the diagnosis of type 2 diabetes, there were willing supportive individuals in place to further assist with the day-to-day management of diabetes.

Microvascular disease was not used as a confounding variable in these analyses. Whereas social support is reliably associated with macrovascular disease, few studies investigate the association between social support and microvascular disease. This is surprising as microvascular complications, for example blindness and amputation, decrease an individual's independence and increase reliance on social contacts. The social networks of these individuals may therefore be instrumental in the successful management of type 2 diabetes. Additionally, a significant proportion of the SOUL-D cohort had microvascular disease but this included microalbuminuria, measured using the albumin to creatinine ratio (ACR). Increased ACR may not elicit social support in

the same way a myocardial infarction might. Microvascular disease develops slowly over a longer period of time whereas a MI is usually a sudden, unexpected event.

7.3.v Main outcome

Glycaemic control at 2 years: Glycated haemoglobin (HbA1c mmol/mol). Values were obtained using the Primus Ultra 2 Bonorate Affinity HPLC (Primus Corporation, 4231 E. 7th Terrace, Kansas City, MO 64132).

7.3.vi Statistical analyses

Data were inputted and descriptive data computed using IBM SPSS version 20.0 (IBM SPSS Inc, Chicago, IL). Adjusted analysis was conducted using Stata 11 (College Station, TX: StataCorp LP). All data were entered and double entered by an external data entry agency. Errors and missing values flagged on data entry were hand checked with original values on questionnaires.

<u>Missing data</u>

The mean of available items was imputed for independent variables of a case (pro-rating) missing < 20% of items (Fox-Wasylyshyn and El-Masri 2005). If ≥ 20% of data on a questionnaire was missing, the summary score was excluded from adjusted analyses.

For community ties, there were 73 cases either missing all data (n = 54) or with incomplete datasets (n = 19). The mean was imputed where 1 item (<20% data) was missing, this was done in 2 cases. If participants had reported having 1 or more

community tie (regardless of the number of values missing) these participants were allocated to the group 'one or more community tie' as they had already reached the threshold score for this group (n = 17) (this is described in the normality paragraphs). There were 54 cases with missing data for this variable, these were excluded from adjusted analyses.

For social network, 116 cases were either missing all data (n = 58) or incomplete (n = 58). The mean response for available items was imputed when 2 items or less (<20% of responses) were missing (n = 30). There were 86 cases with missing social network data who were excluded from adjusted analyses.

For perceived social support there were 79 cases that were either missing all data (n = 69) or were incomplete (n = 9). Mean values were imputed for n = 9 individuals missing 1 item (20% of responses). There were 70 cases missing perceived social support data and these were excluded from adjusted analyses.

Normality in data

For independent variables that were not normally distributed, data were collapsed into categorical variables based on the distribution as data could not be normalised by log or other transformation. Community ties data were positively skewed. Out of 1378 cases, almost half (n = 605) reported having no community ties. Based on the distribution of values, data were categorised into a binary variable: i) no community ties or ii) one or more community ties. Similarly, perceived social support data were negatively skewed and a ceiling effect was observed. Of 1353 available datasets, over half of the sample (n = 866) scored the maximum score (15). Based on the distribution of values, data were again categorised into a binary variable: i) low perceived social

support (0.0 – 12.5) and ii) high perceived social support (12.6 – 15.0). Social network data were normally distributed and used as a continuous variable in analyses.

HbA1c at baseline was positively skewed so the median (IQR) were reported in descriptive analyses.

Descriptive data were summarised as mean (standard deviation) for continuous variables or frequency (percentage) for categorical variables unless data were skewed and reported above.

Unadjusted analyses of the association between social support variables and HbA1c at 2 years were conducted using mixed effects multi-level models to account for the area-level cluster variable of GP. Accounting for the GP may be a proxy for area level factors, such as area level deprivation, or reflect differences in diabetes treatment at the practice level. Adjusted p values are reported in tables alongside descriptive data.

Multivariable mixed effects multi-level models were also used to investigate the independent associations between social support as predictor variables and HbA1c at year 2 as the dependent variable whilst accounting for relevant confounding. GP was again used as the random effects level to account for clustering of participants within GP practices. In the first step, the multi-level model was run using the whole cohort and adjusting for potential confounders: age, gender, ethnicity, employment status, depression status, HbA1c at baseline, diabetes medication and history of macrovascular complications. Unstandardized regression coefficients (b), 95% confidence intervals and p values are reported. The linearity of associations between social support variables and HbA1c was assessed using quadratic terms. The quadratic term was included in the model, if significant, to account for the non-linear association

between risk factor and outcome. In the final step, all confounders, social variables of interest and significant interaction terms were combined into a final multi-level model.

In the second step, analyses were stratified by gender, ethnicity and depression status in order to investigate variations in associations between social support variables and HbA1c. Stratified variables were selected based on existing theory. Models were run separately for stratified variables instead of using the stratification variable and its interaction with other predictor variables in the model for 2 reasons: i) ease of interpretation and ii) risk of too few observations especially in each cell-cell combination of interactions between categorical variables. The proportion of variance explained by the GP which was not explained by the independent fixed factors, was estimated with the interclass correlation (ICC), defined as the ratio of the variance attributable to the GP to the total variance (error variance + variance attributable to patients). The ICC describes how strongly patients within the same GP resemble each other. The greater the ICC, the larger the role of GP in understanding differences in HbA1c.

In the third step, models were formally assessed for possible interactions between social support and stratified variables by rerunning the analyses with the stratification variable and its interaction with social support variables. These associations are reported if significant.

In order to correct for multiple comparisons, the Hochberg improved Bonferroni Method was used. Uncorrected p values are reported in tables but p values will only be discussed as significant if they remain significant after Hochberg's correction. If p values are significant prior to Hochberg adjustments but lose significance they will be treated as trends and only discussed as explorative results.

7.4 **Results**

From 96 GP surgeries, 1447 individuals were recruited between January 2009 and October 2011. Following entry into the study, 14 participants were found to be ineligible and 1 participant withdrew consent. These 15 cases are removed from subsequent analyses. The total sample size used for analyses was 1432. Reasons for participant attrition can be found in the study flow chart,

Figure 17 in Chapter 5.

7.4.vii Baseline characteristics

The baseline characteristics of the first 1432 participants of SOUL-D are summarised in Table 15. The mean age was 56 (±11.06) years, 54% were male and 51%, 38 % and 11% of the sample were white, black and South Asian/other ethnicities respectively. Of the sample, 48% of were in full or part-time employment. At recruitment into the study, the median HbA1c was 48.6 mmol/mol (IQR = 43.17 – 48.63), 54% were on antidiabetic drugs and 9% of participants had a history of macrovascular event. According to the PHQ-9, 15% of participants were depressed.

For structural social support, 55% of participants were married, the mean number of weekly social contacts was 5.8 people (±2.04) (out of a possible 10) and 54% reported being a member of at least one community group, club or organisation. For functional social support, 80% of participants perceived high levels of social support.

Table 15 Main demographic, social and clinical characteristics of the sample at baseline (n = 1432)

Variable	Total*
Age (years)	56.0 (11.06)
Male gender	785 (54.3%)
Ethnicity	
White	725 (50.6%)
Black	546 (38.1%)
South Asian / other	161 (11.2%)
Employment status	
Employed	686 (47.9%)
Unemployed	361 (25.2%)
Retired	385 (26.9%)
Marital status	
Married /cohabiting	804 (56.1%)
Divorced/ separated	196 (13.7%)
Widowed	79 (5.5%)
Single	353 (24.7%)
Community ties	
None	605 (42.2%)
One or more	773 (54.0%)
Social network	5.8 (2.04)
Perceived social support	
Low	210 (14.7%)
High	1152 (80.4%)
Depression status	
Not depressed	1202 (83.9%)
Depressed	211 (14.7%)
Diabetes medication	
Yes	772 (53.9%)
No	638 (44.6%)
Median HbA1c (mmol/mol)	48.6 (43.17 – 48.63)
History of at least 1 macrovascular event	
Yes	132 (9.2%)
No	1276 (89.1%)

For categorical variables, data are presented as n(%) with the exception of HbA1c which is median (IQR). For continuous variables, data are presented as mean (SD); *Percentages may not add up to 100 due to missing data.

In unadjusted analyses (

Table 16 Unadjusted and adjusted associations between social support an covariates and HbA1c (mmol/mol) at 2 years follow-up

Variable	Unadjusted[a]^		Unadjusted^ (n = 873)		Adjusted* (n = 873)	
	b (95% CI)	p value	b (95% CI)	p value	b (95% CI)	p value
Constant					*46.27*	
Age	-0.25 (-0.33, -0.18)	<0.001	-0.24 (-0.31, -0.16)	<0.001	-0.14 (-0.24, -0.04)	0.01
Gender						
Male	1		1		1	
Female	-0.98 (-2.60, 0.64)	0.24	-1.29 (-3.05, 0.48)	0.15	-0.72 (-2.24, 0.89)	0.38
Ethnicity						
White	1		1		1	
Black	1.58 (-0.16, 3.33)	0.08	1.73 (-0.16, 3.64)	0.07	-0.45 (-2.32, 1.43)	0.64
South Asian / other	1.80 (-0.87, 4.46)	0.19	1.59 (-1.32, 4.50)		0.03 (-2.59, 2.66)	0.98
Employment status						
Employed	1		1		1	
Unemployed	-0.98 (-2.97, 1.01)	0.34	-1.95 (-4.13, 0.23)	0.08	-3.15 (-5.30, -0.99)	0.004
Retired	-4.67 (-6.56, -2.79)	<0.001	-4.92 (-6.95, -2.89)	<0.001	-1.58 (-4.06, 0.90)	0.21
Marital status						
Married / cohabiting	1		1		1	
Divorced / Separated	1.35 (-1.03, 3.73)	0.27	1.68 (-0.91, 4.26)	0.20	1.62 (-0.72, 3.97)	0.17
Widowed	-0.97 (-4.41, 2.46)	0.58	-0.12 (-3.88, 3.63)	0.95	2.10 (-1.38, 5.58)	0.24
Single	2.73 (0.79, 4.68)	0.01	2.63 (0.52, 4.73)	0.01	0.72 (-1.21, 2.65)	0.47
Perceived social support						
Low	1		1		1	
High	-2.92 (-5.19, -0.65)	0.01	-3.76 (-6.19, -1.34)	0.002	-2.10 (-4.39, 0.18)	0.07
Community ties						
0	1		1		1	
1 or more	1.53 (-0.14, 3.19)	0.07	1.74 (-0.01, 3.50)	0.05	1.82 (0.09, 3.55)	0.04
Social network	0.18 (-0.23, 0.60)	0.38	0.17 (-0.26, 0.60)	0.44	-0.44 (-0.91, 0.04)	0.07
Depression status						
Not depressed	1		1		1	
Depressed	2.70 (0.39, 5.01)	0.02	2.64 (0.12, 5.16)	0.04	0.86 (-1.52, 3.25)	0.48
Diabetes medication						
No	1		1		1	
Yes	6.95 (5.30, 8.60)	<0.001	7.26 (5.46, 9.07)	<0.001	2.75 (0.94, 4.57)	0.003

Baseline HbA1c (mmol/mol)	0.34 (0.30, 0.40)	<0.001	0.37 (0.32, 0.41)	<0.001	0.32 (0.26, 0.37)	<0.001
History of at least 1 macrovascular event						
No	1		1		1	
Yes	-1.71 (-4.48, 1.06)	0.23	-2.09 (-5.06, 0.87)	0.17	-1.01 (-3.73, 1.70)	0.47

), only accounting for the possible clustering effect of GP, being single was associated with higher HbA1c at 2 years (b = 2.73; CI = 0.79, 4.68) and perceiving high levels of social support was associated with lower HbA1c at 2 years (b = -2.92; CI = -5.19, -0.65). In adjusted analyses after controlling for potential confounders (age, gender, ethnicity, employment status, depression status, diabetes medication, baseline HbA1c and history of microvascular disease) and clustering within GP, having 1 or more community tie was associated with an increase in HbA1c (b = 1.82; CI = 0.09, 3.55). After correcting for multiple testing, this association was not significant. The proportion of the GP explained error variance, estimated with the ICC, was 0.4%.

7.4.viii Stratified analyses

Further analyses aimed to investigate whether there were variations in the association between social support and HbA1c by gender, ethnicity and depression status.

7.4.ix Gender

In unadjusted analyses, social support was not significantly associated with HbA1c at 2 years in males (Table 17). In females, single individuals had significantly higher HbA1c than those married or cohabiting (b = 3.03; CI: 0.20, 5.87) and perceived high levels of support was significantly associated with lower HbA1c (b = -4.06; CI: -7.39, -0.74). In adjusted analyses in males, having one or more community tie was associated with higher HbA1c (b = 2.60; CI = 0.13, 5.07) but having a larger social network was associated with lower HbA1c (b = -0.72; CI = -1.41, -0.03). In females perceiving high levels of social support was associated with lower HbA1c (b = -4.25; CI = -7.54, -0.96).

After correction for multiple testing these associations were not significant. In males, the ICC was 2.1% and in females the ICC was 0.2%.

Table 16 Unadjusted and adjusted associations between social support an covariates and HbA1c (mmol/mol) at 2 years follow-up

Variable	Unadjusted[a]^		Unadjusted^ (n = 873)		Adjusted* (n = 873)	
	b (95% CI)	p value	b (95% CI)	p value	b (95% CI)	p value
Constant					*46.27*	
Age	-0.25 (-0.33, -0.18)	<0.001	-0.24 (-0.31, -0.16)	<0.001	-0.14 (-0.24, -0.04)	0.01
Gender						
Male	1		1		1	
Female	-0.98 (-2.60, 0.64)	0.24	-1.29 (-3.05, 0.48)	0.15	-0.72 (-2.24, 0.89)	0.38
Ethnicity						
White	1		1		1	
Black	1.58 (-0.16, 3.33)	0.08	1.73 (-0.16, 3.64)	0.07	-0.45 (-2.32, 1.43)	0.64
South Asian / other	1.80 (-0.87, 4.46)	0.19	1.59 (-1.32, 4.50)		0.03 (-2.59, 2.66)	0.98
Employment status						
Employed	1		1		1	
Unemployed	-0.98 (-2.97, 1.01)	0.34	-1.95 (-4.13, 0.23)	0.08	-3.15 (-5.30, -0.99)	0.004
Retired	-4.67 (-6.56, -2.79)	<0.001	-4.92 (-6.95, -2.89)	<0.001	-1.58 (-4.06, 0.90)	0.21
Marital status						
Married / cohabiting	1		1		1	
Divorced / Separated	1.35 (-1.03, 3.73)	0.27	1.68 (-0.91, 4.26)	0.20	1.62 (-0.72, 3.97)	0.17
Widowed	-0.97 (-4.41, 2.46)	0.58	-0.12 (-3.88, 3.63)	0.95	2.10 (-1.38, 5.58)	0.24
Single	2.73 (0.79, 4.68)	0.01	2.63 (0.52, 4.73)	0.01	0.72 (-1.21, 2.65)	0.47
Perceived social support						
Low	1		1		1	
High	-2.92 (-5.19, -0.65)	0.01	-3.76 (-6.19, -1.34)	0.002	-2.10 (-4.39, 0.18)	0.07
Community ties						
0	1		1		1	
1 or more	1.53 (-0.14, 3.19)	0.07	1.74 (-0.01, 3.50)	0.05	1.82 (0.09, 3.55)	0.04

Social network	0.18 (-0.23, 0.60)	0.38	0.17 (-0.26, 0.60)	0.44	-0.44 (-0.91, 0.04)	0.07
Depression status						
Not depressed	1		1		1	
Depressed	2.70 (0.39, 5.01)	0.02	2.64 (0.12, 5.16)	0.04	0.86 (-1.52, 3.25)	0.48
Diabetes medication						
No	1		1		1	
Yes	6.95 (5.30, 8.60)	<0.001	7.26 (5.46, 9.07)	<0.001	2.75 (0.94, 4.57)	0.003
Baseline HbA1c (mmol/mol)	0.34 (0.30, 0.40)	<0.001	0.37 (0.32, 0.41)	<0.001	0.32 (0.26, 0.37)	<0.001
History of at least 1 macrovascular event						
No	1		1		1	
Yes	-1.71 (-4.48, 1.06)	0.23	-2.09 (-5.06, 0.87)	0.17	-1.01 (-3.73, 1.70)	0.47

[a] Analyses using all cases for whom data were available, n is variable; ^ Unadjusted analyses accounted for clustering within GP practice only; * Adjusted for all listed variables and clustering within GP practice. CI: Confidence Interval.

7.4.x Ethnicity

When controlling for clustering within GP only (

Table 18, Table 19) in white individuals being divorced or single was significantly associated with higher HbA1c than being married or widowed (b = 3.95; CI: 0.82, 7.09; b = 4.02; CI = 1.51, 6.52 respectively) and perceiving high levels of social support was significantly associated with lower HbA1c (b = -3.11; 95% CI = -5.87, -0.36). Similarly, in South Asian/other individuals, the perception of high levels of social support was associated with lower HbA1c (b = -5.70; CI = -11.11, -0.29). There were no significant associations between social support variables and HbA1c in participants of black ethnicity. In adjusted analyses in white individuals, being divorced or separated was associated with higher HbA1c than those married or cohabiting (b = 3.27; CI = 0.32, 6.22) and in South Asian/other individuals, being widowed was associated with higher HbA1c when compared to married or cohabiting individuals (b = 14.28; CI = 2.00, 26.59). After correction for multiple testing, these associations were no longer significant. In white participants the ICC of GP was 0%, in black participants the ICC was 1.1% and in South Asian / other participants the ICC was 5.6%.

7.4.xi Depression status

When stratified by depression status (

Table 20) and accounting for clustering within GPs, in people who were not depressed, being single was significantly associated with higher HbA1c (b = 2.67; CI = 0.54, 4.79) and perceiving high levels of social support was significantly associated with lower HbA1c (b = -2.82; CI = -5.47, -0.16). In those who were depressed being divorced was significantly associated with higher HbA1c than those who were married (b = 7.90; CI = 1.86, 13.93). When controlling for relevant confounders, a larger social network size was associated with lower HbA1c in those who were not depressed (b = 0.66 CI = -1.17, 0.14) and in depressed participants, being divorced or separated was associated with higher HbA1c than those married or cohabiting (b = 8.12; CI = 1.58, 14.66). These associations were not significant after correction for multiple testing. In those who were not depressed, the ICC of the GP was 1.2% but in depressed participants, ICC was 12.2%.

Interactions between stratified variables and social support measures were investigated using general linear models. All interactions were non-significant ($p > 0.05$) (Appendix V), so the final multi-level model is identical to the model presented in

Table 16 Unadjusted and adjusted associations between social support an covariates and HbA1c (mmol/mol) at 2 years follow-up

Variable	Unadjusted[a]^		Unadjusted^ (n = 873)		Adjusted* (n = 873)	
	b (95% CI)	p value	b (95% CI)	p value	b (95% CI)	p value
Constant					*46.27*	
Age	-0.25 (-0.33, -0.18)	<0.001	-0.24 (-0.31, -0.16)	<0.001	-0.14 (-0.24, -0.04)	0.01
Gender						
Male	1		1		1	
Female	-0.98 (-2.60, 0.64)	0.24	-1.29 (-3.05, 0.48)	0.15	-0.72 (-2.24, 0.89)	0.38
Ethnicity						
White	1		1		1	
Black	1.58 (-0.16, 3.33)	0.08	1.73 (-0.16, 3.64)	0.07	-0.45 (-2.32, 1.43)	0.64
South Asian / other	1.80 (-0.87, 4.46)	0.19	1.59 (-1.32, 4.50)		0.03 (-2.59, 2.66)	0.98
Employment status						
Employed	1		1		1	
Unemployed	-0.98 (-2.97, 1.01)	0.34	-1.95 (-4.13, 0.23)	0.08	-3.15 (-5.30, -0.99)	0.004
Retired	-4.67 (-6.56, -2.79)	<0.001	-4.92 (-6.95, -2.89)	<0.001	-1.58 (-4.06, 0.90)	0.21
Marital status						
Married / cohabiting	1		1		1	
Divorced / Separated	1.35 (-1.03, 3.73)	0.27	1.68 (-0.91, 4.26)	0.20	1.62 (-0.72, 3.97)	0.17
Widowed	-0.97 (-4.41, 2.46)	0.58	-0.12 (-3.88, 3.63)	0.95	2.10 (-1.38, 5.58)	0.24
Single	2.73 (0.79, 4.68)	0.01	2.63 (0.52, 4.73)	0.01	0.72 (-1.21, 2.65)	0.47
Perceived social support						
Low	1		1		1	
High	-2.92 (-5.19, -0.65)	0.01	-3.76 (-6.19, -1.34)	0.002	-2.10 (-4.39, 0.18)	0.07
Community ties						
0	1		1		1	
1 or more	1.53 (-0.14, 3.19)	0.07	1.74 (-0.01, 3.50)	0.05	1.82 (0.09, 3.55)	0.04
Social network	0.18 (-0.23, 0.60)	0.38	0.17 (-0.26, 0.60)	0.44	-0.44 (-0.91, 0.04)	0.07
Depression status						
Not depressed	1		1		1	
Depressed	2.70 (0.39, 5.01)	0.02	2.64 (0.12, 5.16)	0.04	0.86 (-1.52, 3.25)	0.48
Diabetes medication						
No	1		1		1	
Yes	6.95 (5.30, 8.60)	<0.001	7.26 (5.46, 9.07)	<0.001	2.75 (0.94, 4.57)	0.003

Baseline HbA1c (mmol/mol)	0.34 (0.30, 0.40)	<0.001	0.37 (0.32, 0.41)	<0.001	0.32 (0.26, 0.37)	<0.001
History of at least 1 macrovascular event						
No	1		1		1	
Yes	-1.71 (-4.48, 1.06)	0.23	-2.09 (-5.06, 0.87)	0.17	-1.01 (-3.73, 1.70)	0.47

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Table 17 Unadjusted and adjusted analyses of the association between social support at baseline and HbA1c (mmol/mol) at 2 years follow-up, stratified by gender

Variable	Males						Females					
	Unadjusted [a]^		Unadjusted (n = 496)		Adjusted* (n = 496)		Unadjusted [a]^		Unadjusted (n = 377)		Adjusted* (n = 377)	
	b (95% CI)	p value	b (95% CI)	p value	b (95% CI)	p value	b (95% CI)	p value	b (95% CI)	p value	b (95% CI)	p value
Constant					48.63						44.54	
Age	-0.28 (-0.38, -0.18)	<0.001	-0.28 (-0.40, -0.17)	<0.001	-0.20 (-0.35, -0.06)	0.01	-0.23 (-0.33, -0.12)	<0.001	-0.18 (-0.29, -0.07)	0.001	-0.11 (-0.24, 0.02)	0.11
Ethnicity												
White	1		1		1		1		1		1	
Black	2.95 (0.41, 5.48)	0.02	3.16 (0.33, 5.99)	0.03	0.89 (-1.90, 3.69)	0.53	0.58 (-1.86, 3.01)	0.64	0.82 (-1.74, 3.39)	0.52	-1727 (-4.18, 0.73)	0.17
South Asian / other	1.54 (-2.05, 5.13)	0.40	1.56 (-2.40, 5.52)	0.44	-0.35 (-4.02, 3.32)	0.85	2.77 (-1.20, 6.74)	0.17	2.10 (-2.14, 6.34)		0.75 (-2.91, 4.40)	0.69
Employment status												
Employed	1		1		1		1		1		1	
Unemployed	-0.81 (-3.56, 1.94)	0.56	-0.85 (-3.90, 2.20)	0.58	-1.98 (-5.05, 1.08)	0.20	-1.43 (-4.28, 1.41)	0.32	-3.70 (-6.71, -0.69)	0.02	-4.32 (-724, 1.40)	0.004
Retired	-4.18 (-6.82, -1.54)	0.002	-4.23 (-7.14, -1.32)	0.004	0.41 (-3.20, 4.02)	0.85	-5.25 (-7.91, -2.60)	<0.001	-5.88 (-8.62, -3.13)	<0.001	-3.43 (-6.76, 0.10)	0.04
Marital status												
Married / cohabiting	1		1		1		1		1		1	
Divorced / Separated	3.23 (-0.23, 6.69)	0.07	3.39 (-3.38, 7.16)	0.08	2.89 (-0.58, 6.35)	0.10	-0.18 (-3.41, 3.05)	0.91	0.43 (-3.00, 3.86)	0.81	-0.23 (-2.77, 3.23)	0.88
Widowed	-2.58 (-8.98, 3.82)	0.43	-3.46 (-10.64, 3.71)	0.34	0.91 (-5.66, 7.50)	0.78	0.05 (-3.96, 4.06)	0.98	1.98 (-2.23, 6.18)	0.38	2.33 (-1.46, 6.13)	0.23
Single	2.37 (-0.27, 5.01)	0.08	1.59 (-1.32, 4.50)	0.28	0.81 (-1.91, 3.53)	0.56	3.03 (0.20, 5.87)	0.04	3.95 (0.99, 6.91)	0.01	0.90 (-1.83, 3.63)	0.52
Perceived social support												
Low	1		1		1		1		1		1	
High	-1.70 (-4.79, 1.38)	0.28	-2.17 (-5.44, 1.10)	0.19	-0.07 (-3.22, 3.08)	0.97	-4.06 (-7.39, -0.74)	0.02	-5.75 (-9.34, -2.16)	0.002	-4.25 (-7.54, -0.96)	0.01
Community ties												
0	1		1		1		1		1		1	
1 or more	1.86 (-0.41, 4.13)	0.11	1.84 (-0.61, 4.29)	0.14	2.60 (0.13, 5.07)	0.04	1.24 (-1.19, 3.67)	0.32	1.85 (-0.61, 4.31)	0.14	1.81 (-0.58, 4.19)	0.14
Social network	0.04 (-0.52, 0.59)	0.89	-0.02 (-0.61, 0.58)	0.95	-0.72 (-1.41, -0.03)	0.04	0.49 (-0.13, 1.10)	0.12	0.55 (-0.06, 1.15)	0.08	-0.17 (-0.81, 0.47)	0.60

Depression status												
Not depressed	1		1		1		1		1		1	
Depressed	3.78 (0.39, 7.12)	0.03	4.09 (0.42, 7.76)	0.03	2.23 (-1.32, 5.78)	0.22	1.69 (-1.40, 4.79)	0.28	1.15 (-2.19, 4.48)	0.50	-0.99 (-4.07, 2.10)	0.53
Diabetes medication												
No	1		1		1		1		1		1	
Yes	7.72 (5.37, 10.07)	<0.001	8.10 (5.54, 10.68)	<0.001	2.88 (0.21, 5.55)	0.03	6.07 (3.81, 8.34)	<0.001	6.34 (3.85, 8.83)	<0.001	2.23 (-0.13, 4.59)	0.06
Baseline HbA1c (mmol/mol)	0.34 (0.28, 0.41)	<0.001	0.35 (0.28, 0.43)	<0.001	0.29 (0.22, 0.37)	<0.001	0.34 (0.28, 0.42)	<0.001	0.38 (0;31, 0.46)	<0.001	0.34 (0.27, 0.42)	<0.001
History of at least 1 macrovascular event												
No	1		1		1		1		1		1	
Yes	-2.18 (-5.73, 1.38)	0.23	-2.37 (-6.24, 1.51)	0.23	-2.19 (-5.82, 1.44)	0.24	-1.35 (-5.79, 3.09)	0.55	-2.43 (-7.05, 2.18)	0.30	1.28 (-2.85, 5.40)	0.54

[a] Analyses using all cases for whom data were available, n is variable; ^ Unadjusted analyses accounted for clustering within GP practice only; * Adjusted for all listed variables and clustering within GP practice. CI: Confidence Interval.

Table 18 Unadjusted and adjusted analyses of the association between social support at baseline and HbA1c (mmol/mol) at 2 years follow-up in white and black participants

Variable	White						Black					
	Unadjusted [a]^		**Adjusted (n = 477)**		**Adjusted* (n = 477)**		**Unadjusted [a]^**		**Adjusted (n = 302)**		**Adjusted* (n = 302)**	
	b (95% CI)	p value	b (95% CI)	p value	b (95% CI)	p value	b (95% CI)	p value	b (95% CI)	p value	b (95% CI)	p value
Constant					38.64						55.17	
Age	-0.19 (-0.28, -0.09)	<0.001	-0.17 (-2.28, -0.06)	0.002	-0.05 (-0.17, 0.07)	0.46	-0.29 (-0.42, -0.15)	<0.001	-0.25 (-0.40, -0.11)	0.001	-0.25 (0.04, -0.05)	0.01
Gender												
Male	1		1		1		1		1		1	
Female	-0.50 (-2.60, 1.60)	0.64	-0.79 (-3.07, 1.50)	0.50	0.16 (-1.18, 2.15)	0.88	-2.93 (-5.95, 0.09)	0.06	-3.19 (-6.48, 0.10)	0.06	-2.7 (-5.95, 0.54)	0.10
Employment status												
Employed	1		1		1		1		1		1	
Unemployed	-1.08 (-3.75, 1.58)	0.43	-1.40 (-4.30, 1.50)	0.34	-2.61 (-5.41, 0.20)	0.07	-0.54 (-4.11, 3.02)	0.77	-2.26 (-6.13, 1.62)	0.25	-4.37 (-8.41, -0.34)	0.03
Retired	-3.92 (-6.20, -1.64)	0.001	-4.13 (-6.59, -1.66)	0.001	-2.92 (-5.72, -0.12)	0.04	-4.83 (-8.77, -0.90)	0.02	-4.83 (-9.08, -0.58)	0.03	2.13 (-3.42, 7.67)	0.45
Marital status												
Married / cohabiting	1		1		1		1		1		1	
Divorced / Separated	3.95 (0.82, 7.09)	0.01	3.76 (0.36, 7.17)	0.03	3.27 (0.32, 6.22)	0.03	-3.13 (-7.26, 1.00)	0.14	-1.96 (-6.47, 2.54)	0.39	-1.05 (-5.31, 3.20)	0.63
Widowed	-0.74 (-4.59, 3.11)	0.71	0.38 (-3.91, 4.67)	0.86	1.48 (-2.36, 5.32)	0.45	-2.83 (-10.16, 4.51)	0.45	-3.13 (-11.14, 4.87)	0.44	0.94 (-6.72, 8.59)	0.81
Single	4.02 (1.51, 6.52)	0.002	3.45 (0.75, 6.16)	0.01	0.29 (-2.13, 2.71)	0.82	0.50 (-3.02, 4.02)	0.78	0.74 (-3.11, 4.59)	0.70	1.94 (-1.89, 5.77)	0.32
Perceived social support												
Low	1		1		1		1		1		1	
High	-3.11 (-5.87, -0.36)	0.03	-4.08 (-7.05, -1.10)	0.01	-1.37 (-4.11, 1.37)	0.33	-1.32 (-6.05, 3.41)	0.59	-2.66 (-7.56, 2.25)	0.29	2.72 (-7.52, 2.08)	0.27
Community ties												
0	1		1		1		1		1		1	
1 or more	1.15 (-0.91, 3.21)	0.27	1.38 (-0.83, 3.59)	0.22	1.66 (-0.40, 3.73)	0.11	1.80 (-1.67, 5.27)	0.31	2.59 (-1.04, 6.21)	0.16	3.44 (-0.22, 7.10)	0.07
Social network	0.08 (-0.48, 0.63)	0.79	0.02 (-0.56, 0.60)	0.94	-0.53 (-1.13, 0.08)	0.09	-0.03 (-0.780.73)	0.95	0.01 (-0.77, -0.79)	0.98	-0.56 (1.43, 0.30)	0.20
Depression status												
Not depressed	1		1		1		1		1		1	
Depressed	3.58 (0.62, 6.54)	0.02	3.29 (0.06, 6.51)	0.06	1.77 (-1.22, 4.76)	0.25	-0.37 (-4.74, 4.01)	0.87	0.43 (-4.24, 5.10)	0.86	-1.32 (5.91, 3.27)	0.57
Diabetes medication												
No	1		1		1		1		1		1	
Yes	7.03 (5.02, 9.04)	<0.001	7.57 (5.41, 9.72)	<0.001	2.62 (0.48, 4.76)	0.02	7.07 (3.79, 10.36)	<0.001	7.25 (3.38, 11.11)	<0.001	3.39 (-0.49, 7.27)	0.09

Baseline HbA1c (mmol/mol)	0.36 (0.30, 0.42)	<0.001	0.39 (0.33, 046)	<0.001	0.35 (0.29, 0.42)	<0.001	0.30 (0.21, 0.40)	<0.001	0.30 (0.20, 0.39)	<0.001	0.26 (0.16, 0.36)	<0.001
History of at least 1 macrovascular event												
No	1		1		1		1				1	
Yes	-1.85 (-4.80, 1.09)	0.22	-2.88 (-6.07, 0.31)	0.08	-2.52 (-5.33, 0.30)	0.08	-1.42 (-8.69, 5.85)	0.70	0.21 (-7.63, 8.05)	0.96	2.90 (-4.41, 10.20)	0.44

^ Unadjusted analyses accounted for clustering within GP practice only; * Adjusted for all listed variables and clustering within GP practice. CI: Confidence Interval.

Table 19 Unadjusted and adjusted analyses of the association between social support at baseline and HbA1c (mmol/mol) at 2 years follow-up in South Asian participants

Variable	South Asian					
	Unadjusted [a]^		**Unadjusted (n = 94)**		**Adjusted* (n = 94)**	
	b (95% CI)	p value	b (95% CI)	p value	b (95% CI)	p value
Constant					53.36	
Age	-0.41 (-0.63, -0.20)	<0.001	-0.44 (-0.69, -0.21)	<0.001	-0.41 (-0.69, -1.13)	0.004
Gender						
Male	1		1		1	
Female	1.01 (-3.43, 5.47)	0.66	0.08 (-5.00, 5.17)	0.97	1.30 (-3.12, 5.72)	0.57
Employment status						
Employed	1		1		1	
Unemployed	-1.13 (-6.12, 3.86)	0.66	-2.36 (-8.20, 3.48)	0.43	-3.83 (-9.26, 1.60)	0.17
Retired	-6.57 (-12.37, -0.76)	0.03	-7.07 (-13.39, -0.75)	0.03	1.37 (-5.93, 8.67)	0.71
Marital status		0.13				
Married / cohabiting	1		1		1	
Divorced / Separated	5.83 (-1.34, 12.99)	0.11	3.63 (-4.71, 11.99)	0.39	6.41 (-1.01, 13.83)	0.09
Widowed	10.49 (-2.86, 23.84)	0.12	10.72 (-1.77, 10.62)	0.13	14.28 (2.00, 26.59)	0.02
Single	3.70 (-1.73, 9.12)	0.18	4.42 (-1.77, 10.62)	0.16	3.17 (-2.40, 8.75)	0.27
Perceived social support						
Low	1		1		1	
High	-5.70 (-11.11, -0.29)	0.04	-5.56 (-11.92, 0.80)	0.09	-3.82 (-10.15, 2.52)	0.24
Community ties						
0	1		1		1	
1 or more	0.25 (-4.36, 4.86)	0.92	-1.18 (-6.17, 3.81)	0.64	0.54 (-3.98, 5.06)	0.81
Social network	0.63 (-0.65, 1.91)	0.34	0.46 (-0.85, 1.78)	0.49	0.20 (-1.17, 1.57)	0.78
Depression status						
Not depressed	1		1		1	
Depressed	7.19 (1.61, 12.76)	0.01	6.43 (-0.31, 13.17)	0.06	-1.00 (-7.73, 5.72)	0.77
Diabetes medication						
No	1		1		1	
Yes	4.07 (-1.01, 9.15)	0.12	4.47 (-0.90, 9.83)	0.10	-0.21 (-4.99, 5.58)	0.93
Baseline HbA1c (mmol/mol)	0.41 (0.26, 0.56)	<0.001	0.49 (0.32, 0.66)	<0.001	0.41 (0.24, 0.59)	<0.001
History of at least 1 macrovascular event						
No	1		1		1	

Yes	7.29 (-4.50, 19.08)	0.23	9.39 (-2.92, 21.71)	0.14	1.49 (-8.68, 11.66)	0.77

[a] Analyses using all cases for whom data were available, n is variable; ^ Unadjusted analyses accounted for clustering within GP practice only; * Adjusted for all listed variables and clustering within GP practice. CI: Confidence Interval.

Table 20 Unadjusted and adjusted analyses of the association between social support at baseline and HbA1c (mmol/mol) at 2 years follow-up in participants who were not depressed

Variable						
	Unadjusted [a]^		**Unadjusted (n = 751)**		**Adjusted* (n = 751)**	
	b (95% CI)	p value	b (95% CI)	p value	b (95% CI)	p value
Constant					47.74	
Age	-0.26 (-0.34, -0.18)	<0.001	-0.24 (-0.32, -0.16)	<0.001	-0.16 (-0.27, -0.06)	0.002
Gender						
Male	1		1		1	
Female	-0.80 (-2.56, 0.95)	0.37	-0.93 (-2.80, 0.94)	0.33	-0.31 (-1.99, 1.37)	0.72
Ethnicity						
White	1		1		1	
Black	2.10 (0.24, 3.97)	0.03	2.11 (0.10, 4.11)	0.04	0.34 (-.63, 2.31)	0.73
South Asian / other	1.04 (-1.90, 3.98)	0.49	1.08 (-2.01, 4.17)	0.49	0.01 (-2.75, 2.77)	1.00
Employment status						
Employed	1		1		1	
Unemployed	-0.86 (-3.15, 1.44)	0.46	-1.93 (-4.40, 0.53)	0.13	-3.90 (-6.23, -1.57)	0.001
Retired	-4.22 (-6.18, -2.27)	<0.001	-4.30 (-6.38, -2.22)	<0.001	-1.48 (-4.03, 1.08)	0.26
Marital status						
Married / cohabiting	1		1		1	
Divorced / Separated	-0.27 (-2.88, 2.34)	0.84	0.23 (-2.56, 3.01)	0.87	0.37 (-2.13, 2.86)	0.77
Widowed	-1.47 (-5.14, 2.20)	0.43	-0.54 (-4.58, 3.50)	0.79	1.86 (-1.83, 5.55)	0.32
Single	2.67 (0.54, 4.79)	0.01	2.57 (0.31, 4.84)	0.03	0.65 (-1.38, 2.68)	0.53
Perceived social support						
Low	1		1		1	
High	-2.82 (-5.47, -0.16)	0.04	-4.04 (-6.88, -1.21)	0.01	-1.93 (-4.50, 0.63)	0.14
Community ties						
0	1		1		1	
1 or more	1.54 (-0.24, 3.32)	0.09	1.85 (-0.02, 3.72)	0.05	1.71 (-0.11, 3.53)	0.07
Social network	0.14 (-0.31, 0.59)	0.54	0.12 (-0.35, 0.58)	0.63	-0.66 (-1.17, 0.14)	0.01
Diabetes medication						
No	1		1		1	
Yes	6.57 (4.83, 8.30)	<0.001	6.79 (4.91, 8.67)	<0.001	2.10 (0.24, 3.96)	0.03
Baseline HbA1c	0.36 (0.31, 0.41)	<0.001	0.38 (0.33, 0.44)	<0.001	0.34 (0.28, 0.40)	<0.001

(mmol/mol)						
History of at least 1 macrovascular event						
No	1		1		1	
Yes	-1.92 (-5.00, 1.16)	0.22	-2.02 (-5.26, 1.22)	0.22	-0.62 (-3.54, 2.31)	0.68

[a] Analyses using all cases for whom data were available, n is variable; ^ Unadjusted analyses accounted for clustering within GP practice only; * Adjusted for all listed variables and clustering within GP practice. CI: Confidence Interval.

Table 21 Unadjusted and adjusted analyses of the association between social support at baseline and HbA1c (mmol/mol) at 2 years follow-up in participants who were depressed

Variable						
	Unadjusted [a]^		**Unadjusted (n = 751)**		**Adjusted* (n = 122)**	
	b (95% CI)	p value	b (95% CI)	p value	b (95% CI)	p value
Constant					35.00	
Age	-0.08 (-0.34, 0.18)	0.56	-0.11 (-0.40, 0.17)		0.07 (-0.28, 0.42)	0.68
Gender						
Male	1		1		1	
Female	-2.82 (-7.36, 1.72)	0.22	-3.40 (-8.44, 1.64)	0.19	-3.77 (-8.68, 1.13)	0.13
Ethnicity						
White	1				1	
Black	-1.95 (-6.87, 2.97)	0.44	-0.67 (-6.10, 4.77)	0.81	-1.88 (-7.42, 3.67)	0.51
South Asian / other	3.54 (-3.29, 10.37)	0.31	2.58 (-5.63, 10.90)	0.54	0.60 (-7.04, 8.42)	0.88
Employment status						
Employed	1		1		1	
Unemployed	-3.45 (-8.29, 1.39)	0.16	-5.09 (-10.49, 0.31)	0.06	-1.09 (-6.89, 4.71)	0.71
Retired	-7.04 (-14.29, 0.22)	0.06	-9.95 (19.66, 2.23)	0.01	-7.14 (-15.85, 1.57)	0.12
Marital status						
Married / cohabiting	1		1		1	
Divorced / Separated	7.90 (1.86, 13.93)	0.01	8.51 (1.61, 15.42)	0.02	8.12 (1.58, 14.66)	0.02
Widowed	3.01 (-6.31, 12.33)	0.53	2.97 (-6.66, 12.62)	0.55	3.13 (-6.76, 13.01)	0.54
Single	3.13 (-2.01, 8.28)	0.23	2.52 (-3.21, 6.25)	0.39	2.52 (-3.39, 8.42)	0.40
Perceived social support						
Low	1		1		1	
High	-0.93 (-5.74, 3.88)	0.71	-0.93 (-6.11, 4.25)	0.72	-3.20 (-8.51, 2.10)	0.24
Community ties						
0	1		1		1	
1 or more	3.60 (-1.05, 8.26)	0.13	3.35 (-1.71, 8.41)	0.20	3.16 (-1.87, 8.19)	0.22
Social network	0.82 (-0.24, 1.89)	0.13	0.92 (-0.20, 2.04)	0.11	0.92 (-0.34, 2.17)	0.15
Diabetes medication						
No	1		1		1	

Yes	8.19 (2.95, 13.44)	0.002	9.48 (3.50, 15.46)	0.002	6.51 (0.54, 12.48)	0.03
Baseline HbA1c (mmol/mol)	0.25 (0.11, 0.39)	0.001	0.25 (0.10, 0.41)	0.002	0.15 (-0.12, 0.32)	0.08
History of at least 1 macrovascular event						
No	1		1		1	
Yes	-0.48 (-7.16, 6.21)	0.88	-2.05 (-9.45, 5.36)	0.59	-3.08 (-10.50, 4.35)	0.42

[a] Analyses using all cases for whom data were available, n is variable; ^ Unadjusted analyses accounted for clustering within GP practice only; * Adjusted for all listed variables and clustering within GP practice. CI: Confidence Interval.

7.5 **Discussion**

This prospective study investigated the association between functional and structural social support at baseline and glycaemic control at 2 years in individuals with newly diagnosed type 2 diabetes.

Social support was not a significant predictor of HbA1c at 2 years; however there were a number of statistical trends which must be interpreted with caution but may warrant further investigation. Membership of community organisations was associated with higher HbA1c and, on stratification by gender, in males. These associations were in the opposite direction than hypothesised. A larger social network was associated with lower HbA1c in males and in those who were not depressed. Being divorced was associated with higher HbA1c in white individuals and in those who were depressed. In South Asian / other ethnicities, being widowed was associated with higher HbA1c. For functional support, the perception of high levels of support was associated with lower HbA1c in female participants.

However there is no clear social patterning or identifiable trend across social support measures. Our findings may therefore add to previous research, which suggests that the widely documented protective effect of social support on biomedical outcomes is not so evident in individuals with type 2 diabetes (van Dam et al. 2005, Stopford et al. 2013). There are three possible explanations for this observed lack of association:

Firstly, social support may not be an important construct in relatively healthy individuals with type 2 diabetes. Our study included participants with a new diagnosis of type 2 diabetes, the majority asymptomatic at diagnosis and few presenting with complications (Winkley et al. 2013), glycaemic control at 2 years follow-up was also reasonable (median = 48.6 mmol/mol). The recently diagnosed nature of the sample

makes these individuals clinically similar. It may therefore be too early to observe an effect of social support on HbA1c. For most, type 2 diabetes does not present as an emergency and, although progressive, is relatively stable in the medium term. The increasing prevalence of type 2 diabetes, and the slow progressing nature of the disease, may not 'activate' social support from social networks in the same way a diagnosis of cancer or a cardiovascular event might. The diabetes literature reports that it is the physical symptoms which act as indicators that support may be needed (Iida et al. 2010). This study excluded people with advanced complications, an effect of social support may not be seen until health deteriorates and complications develop with disease progression and disability. Similarly, if a patient does not perceive diabetes as a serious concern or believes that the public view of diabetes is not sympathetic or supportive, s/he may be unwilling to access or utilise existing support resources (van Dam et al. 2005). Utilising such support might also reduce an individual's sense of autonomy or be perceived as weak. Studies recruiting participants from primary care or outpatient settings may under-sample individuals experiencing complications. This may result in an underestimation of the effect of social support on diabetes outcomes.

Secondly, individuals with type 2 diabetes may be a distinct group who have less social support than the general population. Poor social support may contribute to the development of type 2 diabetes rather than the management of the disease. Although research is limited, two Scandinavian studies found that people with type 2 diabetes had poorer social relations, were more likely to live without a partner and without contact with family than population controls (Hempler et al. 2013, Aalto et al. 1996). Additionally in the non-diabetic population, poor social support has been associated with impaired glucose metabolism (Feldman and Steptoe 2003).

Thirdly, despite the presence of social support in type 2 diabetes, the assistance provided may not necessarily be supportive. In our cohort, there were significant ranges on social support measures (excluding community ties) and the social network

data resemble those of previous research utilising similar measures (Cornwell and Waite 2009, Chlebowy and Garvin 2006). We can infer that there is evidence of existing social support structures in our sample, but the functional components of support may not be elicited or effective. Generally, literature on the influence of family friends on chronic disease management reports positive effects, however hindrance has also been reported, particularly from family members (Gallant et al. 2007). Mayberry at al. found that individuals with type 2 diabetes felt 'sabotaged' by family members who were well informed about diabetes (Mayberry and Osborn 2012). 'Miscarried help', the notion that helping behaviours infringe upon self-efficacy, was also a theme elicited from focus groups about family involvement in diabetes self-management. It is a concept associated with rebellion and often described in the adolescent literature but may also be applicable to adults. Participants also reported that they received unwanted assistance, and felt nagged or threatened to perform self-care behaviours from family members. This finding may reflect the discretionary nature of friendships; that non-supportive friends are more likely to be abandoned than non-supportive familial relationships (Gallant et al. 2007).

Strengths of the study are that it used a large, representative, multi-ethnic cohort and extensive dataset that was able to simultaneously examine multiple constructs of social support. It is a unique cohort recruited immediately after the diagnosis of type 2 diabetes and commencement of treatment. It is also one of the few medium-sized cohorts with prospective data.

However, it would be useful to have a non-diabetes control group with which to compare this cohort. This would allow us to contrast the levels of social support and replicate findings from the two Scandinavian studies previously discussed (Hempler et al. 2013, Aalto et al. 1996), in an inner-city setting in the UK. It would be hypothesised that the SOUL-D cohort would have lower levels of social support than the general population which may indicate that low levels of social support contribute more significantly to the development of diabetes. It would also be of interest to compare

the SOUL-D cohort to individuals with other long term conditions, such as arthritis. There is a general perception that individuals with type 2 diabetes are partially accountable for the onset of the disease, this is also the case for obesity. However, this may not be the case with arthritis. Support may therefore be more readily available and helpful in individuals with arthritis when compared to type 2 diabetes. Drawing comparisons between general population and long term condition control groups may allow us to develop social support theory. Psychological factors of the support-giver such as hostility, resentment and shame might play a larger role in some diseases than initially hypothesised.

Methodological issues in the social support literature have been reported since the early 1980s; the conceptual definition of social support, the heterogeneity of measures and lack of reliable and valid measures (O'Reilly 1988). Many have critiqued the 'persistent vagueness' of measures used to define and conceptualise social support and there is still no consensus as to a 'gold standard' assessment tool. In our study, the social network variable quantitatively scored the number of weekly contacts but did not take into account the frequency, utility or benefit of contacts. Although the variables assessed whether social support was perceived to be available, they did not measure the quality of social relationships. This may be an important omission as negative support, such as nagging and criticism, may be more strongly predictive of health outcomes (Clark and Nothwehr 1997). Furthermore, being married is not universally beneficial. The satisfaction, quality and support provided by the relationship is important; single people are reported to have better health status compared to those who are unhappily married (Holt-Lunstad et al. 2008). The change in social support over the study period was not assessed. In order to do this, more covariates would need to be added to regression models thus reducing power. The rationale for not doing this was the assumption that social support is relatively stable with little change over 2 years.

Investigating the association between social support and glycaemic control in type 2 diabetes is necessary when identifying modifiable targets of intervention beyond traditional risk factors. These results suggest that the beneficial effect of social support observed in the wider health literature may not directly translate to individuals with type 2 diabetes. They also provide tentative evidence for demographic variations in any association between social support and glycaemic control, however these findings must be interpreted with caution.

The next chapter reports the prospective association between the proximal neighbourhood environment and glycaemic control at 2 years.

Chapter 8 The neighbourhood and glycaemic control: a prospective analysis

8.1 **Synopsis**

In Chapter 7 there was little evidence for an association between social support at an individual level and HbA1c in type 2 diabetes. The aim of this chapter is to investigate the association between the neighbourhood factors, primarily at an area level, and glycaemic control in individuals 2 years post diagnosis of type 2 diabetes.

The neighbourhood environment is associated with morbidity and mortality. It has also been associated with increased diabetes prevalence (Cox et al. 2007) and insulin resistance in the healthy population (Auchincloss et al. 2008) but it is not known if there is a prospective association between the neighbourhood and glycaemic control in type 2 diabetes. In order to investigate this association, the SOUL-D cohort was used again. Neighbourhood variables were matched to participant postcode at baseline. Area level neighbourhood factors were measured using: i) the Index of Multiple Deprivation (IMD); ii) violent crime; iii) policing and iv) the obesogenic environment (distance to recreational facilities and green space and density of fast food outlets). Individual level neighbourhood factors were measured using perceptions of the neighbourhood environment. The main outcome was glycaemic control (HbA1c (mmol/mol)) at 2 years. From 96 GP surgeries, 1447 individuals with newly diagnosed type 2 diabetes were recruited. In a mixed-effects multi-level model, neighbourhood variables were not independently associated with HbA1c at 2 years adjusting for baseline HbA1c. In contrast to previous research of established diabetes, this study suggests that the neighbourhood environment is not important for people with newly

diagnosed type 2 diabetes. However, a longer term follow-up is necessary to investigate whether any association emerges following a longer duration of living with a chronic condition, complications and disability.

8.2 **Introduction**

Chapter 4 reviewed the evidence for a role of the neighbourhood environment in health and found that limited evidence exists in type 2 diabetes. The key points from the literature review can be summarised as follows:

The neighbourhood environment plays a significant role in producing and maintaining health inequalities (Pickett and Pearl 2001). Adverse neighbourhood environments are associated with morbidity and mortality independently of individual socio-economic status. The neighbourhood environment is also associated with chronic disease and lifestyle behaviours (Diez Roux et al. 2002, Gary et al. 2008).

In type 2 diabetes, the necessary lifestyle changes are often complex and may not be sustainable in unsupportive environments. Deprived neighbourhoods, high levels of crime and obseogenic environments (neighbourhoods which foster low levels of physical activity and ease of access to energy-rich foods) may influence an individual's ability to engage in healthy lifestyle behaviours (Roux et al. 2007, Leal and Chaix 2010).

However, few studies have investigated the role of the neighbourhood in type 2 diabetes and its association with glycaemic control and, to the best of my knowledge, the studies that have are all cross-sectional. In the US, the perception of neighbourhood problems was inversely associated with participation in physical activity in a cross-sectional study of participants type 2 diabetes (Gary et al. 2008) and in the DISTANCE Study, again in the US, neighbourhood deprivation was independently

associated with poor glycaemic control (Laraia et al. 2012). This finding was also reported in California using Geographic Information Systems (GIS) (Geraghty et al. 2010). Greater resources for physical activity are independently associated with lower insulin resistance (Auchincloss et al. 2008), but at the time of writing there are no published studies investigating a prospective association between the built neighbourhood environment and glycaemic control in type 2 diabetes.

Methodological challenges are frequently reported. Macintyre and colleagues (2002) describe the neighbourhood as a 'black box of somewhat mystical influences on health' (Macintyre et al. 2002). Many studies use aggregate neighbourhood measures, at varying spatial levels, as the sole measure of neighbourhood characteristics and fail to quantify specific neighbourhood attributes (Diez Roux 2003) or incorporate subjective measurements. In order to capture individual neighbourhood attributes, specific environmental and neighbourhood domains (for example, crime, policing, access to healthcare) should be used in the place of global summary measures to refrain from classing 'neighbourhoods' as another single feature in epidemiological webs of causation (O'Campo 2003). These studies, advancing on earlier methodologies, have been termed the 'second generation of neighbourhood health effects studies' (Diez Roux and Mair 2010).

The aims of this study are to investigate i) whether the area level social neighbourhood environment (IMD, crime and policing) is associated with HbA1c at 2 years; ii) whether the individual level social neighbourhood environment (neighbourhood perceptions) is associated with HbA1c at 2 years; iii) whether the obesogenic environment (access to green space and recreational facilities, and density of fast food outlets) is associated with HbA1c at 2 years and iv) whether the association between neighbourhood characteristics and HbA1c is mediated by self-care behaviours (diet and exercise).

Hypotheses

1. Neighbourhood deprivation and crime levels will be associated with higher HbA1c.
2. High levels of policing will be associated with lower HbA1c.
3. Increasing distance to green space and recreational facilities and higher density of fast food outlets will be associated with higher HbA1c.
4. Any association will be mediated by lifestyle factors (diet and exercise).

8.3 **Methodology**

8.3.i Design

As in the previous chapter, this chapter uses prospective data from the SOUL-D cohort.

8.3.ii Setting and Sample

SOUL-D recruited from 3 multi-ethnic and socio-economically diverse boroughs of South East London. The sample included individuals with newly diagnosed (< 6 months duration) type 2 diabetes.

8.3.iii Explanatory variables

Full details of explanatory variables are reported in chapter 5.

Area level factors

All data were matched to participant postcode at baseline.

Social neighbourhood environment

i) The Index of Multiple Deprivation (IMD 2007) is an aggregate measure of relative neighbourhood deprivation reflective of the circumstances and lifestyles of individuals across 7 domains: income, employment, health and disability, education skills and training, barriers to housing and other services, crime and living environment.

ii) Violent crime: This was classified as violence against the person, sexual offences and robbery (Metropolitan Police 2013). Data on sexual offences are withheld. Higher figures represent higher levels of violent crime.

iii) Number of police officers: The total number of police and community support officers was calculated from the Metropolitan Police website where data are publicly available (Metropolitan Police 2013). These data were available at ward level. Participant postcode was matched to ward which was matched to police data.

Data were not always available at the smallest neighbourhood level required which was LSOA. Policing data were available at ward level, a significantly larger administratively defined geographical area which, may represent a less accurate measurement of the neighbourhood. However, residents remain exposed to this feature of the social environment albeit at a more macro-level (Cummins et al. 2005a). As there are multiple LSOAs within each ward, a criticism of this approach is that LSOAs

will have been ascribed the same value even though levels of exposure (distribution in allocation of police resources) may not be equally distributed throughout wards. Ward level data on this particular variable were the most precise and best measure available.

Individual level factors

i) Perception of neighbourhood disorder. Participants were asked: 'thinking about where you live, how much of a problem is each of the following: crime, access to exercise facilities, rubbish and litter, lighting at night, access to transportation, access to nearby supermarket, vandalism/graffiti, safety?' Each item had four possible responses (very serious problem, somewhat serious problem, minor problem and not a problem) (Gary et al. 2008). Higher scores indicate perception of fewer neighbourhood problems.

Measures of the obesogenic environment

Area level factors

Residential locations were mapped using ArcGIS 9.2 Geographical Information Systems (ESRI, California). The distance in metres from participant postcode to green space and recreational facilities and the density of fast food outlets in the proximate neighbourhood were computed. The process is described in Chapter 5. The following definitions were used:

1) Green space: areas in which physical activity could potentially be undertaken and are free to use, for example, parks and commons.

2) Recreational facilities: facilities used to participate in indoor or outdoor sports, facilities which had indoor gymnasiums or had facilities with specialist equipment for one sport. Recreational facilities usually require a fee to use, for example, sports halls and leisure centres.

3) Fast food outlets: a retailer selling hot food for consumption on, or off, the premises, for example, fast-food and takeaway outlets. These are in contrast to full service restaurants.

The proximate neighbourhood was defined as the area within 400 metres along the road network from participant postcode. This equates to a 5 - 6 minute walk.

8.3.iv Potential confounders

It is assumed that neighbourhood effects operate homogenously across sub-populations of society (van Ham et al. 2012) but there is evidence that the following variables may modify any association. These variables were regarded as confounders in the association between the neighbourhood environment and health.

Age (years). Age may be a significant determinant of how individuals utilise their neighbourhood environment. Elderly individuals, particularly those who are less mobile, may be more reliant on their neighbourhoods (Macintyre et al. 2002). These individuals may therefore be influenced to a greater extent by the resources within ones neighbourhood and more susceptible to the influence of neighbourhood crime and deprivation. Stay at home females with young children may be similarly influenced by the proximate neighbourhood environment. This would be in contrast to employed

adults of a working age, many of whom may travel outside of their neighbourhood to their place of employment. Conversely, compared to younger individuals, older adults, particularly healthy older adults, may have fewer time constraints (for example, due to retirement) and may choose to travel to adjacent neighbourhoods or shopping areas rather than rely on services provided in their neighbourhood. These individuals may therefore be less susceptible to the influence of the neighbourhood environment.

Gender: male / female. Gender differences are observed in associations between the neighbourhood environment and health. Males and females have different perceptions of the neighbourhood environment (Mohai 1997) which may influence their use of certain resources (O'Brien 2005). For example, females report feeling significantly more uncomfortable in neglected or derelict areas and report concerns for their safety when using green spaces that are not obviously managed. In contrast, males have more of a preference for remote settings for recreational activity. These gender differences may, in part, result from gender roles. Females may be more dependent on local amenities than males, when staying at home and raising children for example, and may therefore be more exposed to the effects of the neighbourhood environment. However, in a cross-sectional study of contrasting neighbourhoods in Glasgow, UK, gender differences in neighbourhood perceptions were not explained by time spent in the local area (measured by employment status) but were partially explained by having children living at home (Ellaway et al. 2001).

Self-reported ethnicity: white, black or South Asian/other. Ethnic differences are observed in neighbourhood perceptions but these are varied and contrasting. Ethnic minority groups have been suggested to hold more positive neighbourhood perceptions than white people who are more likely to express dissatisfaction with their environment (Karlsen et al. 2002). In contrast, Elo and colleagues reported no difference in perceptions in white and black individuals (Elo et al. 2009). Also, certain neighbourhoods may display 'resilience' despite high levels of deprivation (Karlsen et al. 2002). These areas are often comprised of ethnic minority populations (Doran et al.

2006). The 'ethnic density effect' purports that the lower the concentration of an individual's ethnic group, the worse the health outcomes (Halpern and Nazroo 2000). The presence of community and extended networks of social support (larger in ethnic minority groups) may also distract from factors such as crime, dereliction and violence, which are associated with areas of deprivation thus lessening the effects of these variables on health outcomes.

National Statistics Socio-Economic Classification (NS-SEC): A proxy for individual socio-economic status. Five categories were used: i) managerial, administrative and professional occupations ii) intermediate occupations iii) small employers and own account workers iv) lower supervisory and technical occupations and v) semi-routine and routine occupations. Individuals of low socio-economic status may be dependent on their area of residence due to lack of car ownership and reliance on public transport. The established association between socio-economic status and health outcomes renders socio-economic status a key confounder in aetiological analyses. Additionally, it is of interest and significant importance for policy development and resource allocation to establish whether the neighbourhood environment is associated with HbA1c independently of an individual's socio-economic status, although there may be correlation between these two constructs.

Depression status: measured using the Patient Health Questionnaire – 9 (PHQ-9) (Spitzer et al. 1999). A value ≥ 10 indicates the likelihood of depression. Neighbourhood deprivation is associated with depression and depressive symptomology in both cross-sectional and longitudinal studies (Ross 2000, Mair et al. 2008). Possible explanations for this association are that a lack of resources, crime and violence, derelict housing and lack of, or inadequate, green space act as stressors and may affect depressed individuals in a more detrimental way than individuals who are not depressed. People with depression experience low mood, anhedonia and feelings of hopelessness. Living in deprived neighbourhoods with limited resources may simply attenuate these feelings. The social withdrawal seen in people with depression may

also increase reliance on the proximate environment. The Neighbourhood Perceptions Questionnaire may be particularly influenced by depression. A depressed individual may view their neighbourhood in a more negative light regardless of objective measures of neighbourhood quality. In type 2 diabetes it is well established that depression is associated with sub-optimal diabetes self-care and glycaemic control (Ciechanowski et al. 2000).

Antidiabetic agents: *i*) prescribed oral antidiabetic agents or insulin or ii) not prescribed any diabetes medication. Individuals living in certain neighbourhoods may be more likely to be prescribed anti-diabetic medication at the diagnosis of type 2 diabetes. This may reflect differences in prescribing practices at GP surgeries or other factors (for example a preference to adapt lifestyle behaviours in the first instance) that may influence the physician's decision to prescribe medication to certain groups of individuals.

Previous macrovascular event was defined as a history of: myocardial infarction, coronary artery bypass graft, cerebrovascular accident and carotid or limb revascularisation. This was self-reported and validated from medical records. Epidemiological research associates neighbourhood socio-economic status with cardiovascular risk factors (hyperlipidaemia, BMI and hypertension) and cardiovascular events (Smith et al. 1998). Deprived neighbourhoods also demonstrate a higher prevalence of cardiovascular related mortality, an association that remains after controlling for individual socio-economic status (Diez Roux 2003, Roux et al. 2001). In the SOUL-D cohort it may be that individuals who had had a previous macrovascular event had already been subject to the effects of their neighbourhood environment or were individuals who were more susceptible to these external stressors. In type 2 diabetes it is known that the risk of macrovascular complications is significantly associated with previous hyperglycaemia. However, following a macrovascular event

we may expect individuals to have better glycaemic control due to frequent monitoring and increased professional support.

8.3.v Mediators

Diabetes self-management was assessed using two subsections: diet and exercise, of the Summary of Diabetes Self-Care Activities measure (SDSCA)(Toobert et al. 2000). For diet, the SDSCA assesses adherence to general diet (2 items) and adherence to dietary recommendations (2 items): eating five or more servings of fruit and vegetables a day and eating high-fat foods. Exercise levels were assessed by asking participants on how many of the last seven days they participated in at least 30 minutes (continuous) of physical activity and on how many days they participated in a specific exercise session. Responses ranged from 1 – 7 days per week. Diet and exercise are considered important components of the self-management of diabetes. They can improve insulin sensitivity, glycaemic control and reduce the need for antidiabetic drugs.

8.3.vi Main outcome

Glycaemic control at 2 years: Glycated haemoglobin (HbA1c mmol/mol). Values were obtained using the Primus Ultra 2 Bonorate Affinity HPLC (Primus Corporation, 4231 E. 7th Terrace, Kansas City, MO 64132).

8.3.vii Statistical analyses

Data were input and unadjusted analyses conducted using IBM SPSS version 20.0 (IBM SPSS Inc, Chicago, IL). Adjusted analysis was conducted using Stata 11 (College Station,

TX: StataCorp LP). All data were double entered by an external agency. Missing or ambiguous data were hand checked with original data collection schedules.

Missing data

The mean of available items was imputed for independent variables of a case (pro-rating) missing < 20% of items (Fox-Wasylyshyn and El-Masri 2005). If ≥ 20% of data on a questionnaire were missing, the summary score was excluded from analyses. For the neighbourhood perceptions questionnaire, values were imputed for cases missing <20% (one item) from the 8 item scale. Out of 81 cases missing data, 14 cases were missing 1 response and the mean of available items was imputed. There were 47 cases missing all responses for this questionnaire. After imputation, there were 67 cases with missing data and these were excluded from analyses.

All other independent variables were obtained through external agencies and matched to participant postcode at baseline which minimised the risk of missing data. After 2 years, 122 participants (8.5% of the total cohort) had moved; 67 (4.7%) had moved within London, 26 (1.8%) had moved outside London, 20 (1.4%) could not be traced and 9 (0.6%) had moved out of the UK. Analyses were conducted with and without these individuals in the dataset. There were no differences in statistical results and so these participants remained in the dataset. There were 405 participants (28.3% of the sample) missing HbA1c data at year 2. These cases were excluded from analyses.

Normality in data

Data were checked for normality. For skewed independent variables, data were collapsed into categories based on distributions using visual binning as data could not

be normalised by log or other transformation. Visual binning allows for the categorisation of continuous or ordinal variables based on visible groups or clusters of the variable. For the purpose of analysis, the IMD ranks were divided into two groups (1 = least deprived and 2 = most deprived). The IMD ranks of participants clustered amongst the lower ranks (most deprived) when compared to the national range. Creating groups based on the national spread of deprivation ranks was therefore not feasible.

Based on the distribution of values, for green space, the following categories were used: i) <100m; ii) 100 - 199m; iii) 200 - 299m; and iv) ≥300m. For recreational facilities the following categories were used: i) <120m; ii) 120 - 239m; iii) 240 - 359m; and iv) ≥360m. Fast food restaurants were normally distributed and were used as a continuous variable in analyses.

The neighbourhood perceptions data were negatively skewed. Over half of the sample (n = 846) scored either 31 or 32 out of a possible 32. Based on the distribution of values, total scores were collapsed into a binary variable (1 (least neighbourhood problems) = 0-29; or 2 (most neighbourhood problems) = 30-32).

Descriptive statistics

Descriptive data were summarised as mean (standard deviation) or frequency (percentage). For HbA1c at baseline, the median (IQR) was reported.

Unadjusted analyses of the associations between neighbourhood variables and HbA1c were conducted using mixed effects multi-level models to account for clustering within GP practice. These analyses were run using i) the whole cohort for whom data were

available for each association and ii) the restricted sample included in the adjusted model.

Mixed effects multi-level models were also used to investigate associations between neighbourhood variables and HbA1c at year 2. The model was adjusted for potential confounders: age, gender, ethnicity, NS-SEC (individual socio-economic status), depression status, baseline HbA1c, diabetes medication and history of macrovascular complications. General practitioner was used as the random effects level to account for clustering of participants within GP practices. As discussed in Chapter 7, the GP is a proxy for neighbourhood characteristics and differences in healthcare, prescribing practices for example. The proportion of variance explained by the GP was estimated with ICC defined as the ratio of the variance attributable to the GP to the total variance (error variance + variance attributable to patients). The ICC describes how strongly patients within the same GP resemble each other. For the unadjusted and adjusted analyses, unstandardized regression coefficients (b), 95% confidence intervals and p values are reported.

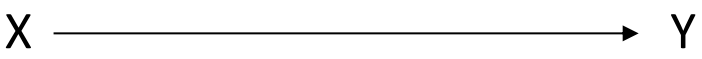
The Hochberg improved Bonferroni method was used to correct for multiple comparisons. Uncorrected p values are reported in tables but p values will only be discussed as significant if they remain significant after Hochberg's correction. If p values are significant prior to Hochberg adjustments but then lose significance they will be treated as trends and discussed as explorative results.

Mediational analysis

In order to investigate the mechanistic route of action of any association, mediational analyses were used. A mediational model is a hypothesized causal process that seeks to identify a process explaining an observed association between an independent

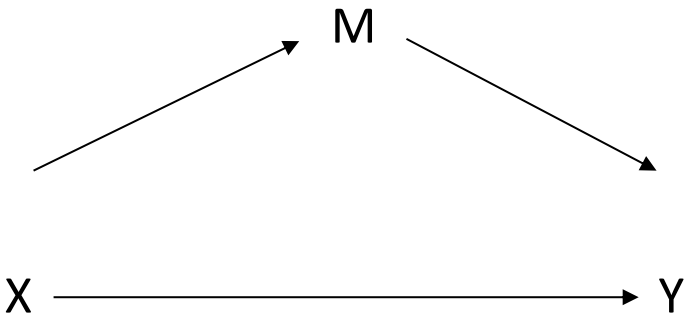
variable and a dependent variable. In this thesis, it is proposed that diet and exercise will mediate any association between neighbourhood factors and glycaemic control. These factors are therefore not used as confounders in the multi-level analyses.

Graphically, mediation can be depicted in the following way:



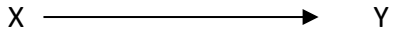
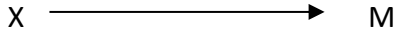
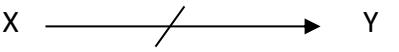
It is proposed that variable X is associated with variable Y, where variable X is the causal variable (independent variable). Pathway C is the total effect. This diagram represents an unmediated model.

The mediator (M) is a process variable, which may explain the association between X and Y. Partial mediation occurs when the association of the path from X to Y is reduced (but still differs from zero) when the mediator is introduced. The amount of mediation is the indirect effect.



The mediator (M) is hypothesized to cause the outcome (Y) and not vice versa. Statistical analysis can be used to test a mediational model. The four main statistical steps and assumptions of establishing mediation are detailed (Baron and Kenny 1986).

Table 22 The four steps of mediational analysis

	Analysis	**Diagrammatic explanation**
Step 1	Demonstrate that the causal variable (X) is associated with the outcome (Y). This step establishes that there is an association to be mediated.	
Step 2	Demonstrate that the causal variable is associated with the mediator, where X is the predictor (independent) variable and M is the dependant variable in the regression equation.	
Step 3	Show that the mediator is associated with the outcome variable (Y) (independently of X). Use M and X as the independent variables and Y as the dependant variable in regression analysis. A simple correlation is not sufficient in establishing an association. They may be correlated as both are associated with independent variable X. Variable X must therefore be controlled when testing the effect of M on Y.	 Controlling for X
Step 4	To establish complete mediation by M, the effect of X on Y when controlling for M should be zero.	 Controlling for M

Where ⟶ assumes an association

It is debated whether all the steps have to be met for mediation to take place. If all four steps are met, then complete mediation by variable M is indicated. If the first three steps, but not the fourth step, is met, then partial mediation has taken place. If one or more of the assumptions in steps one to three are not met then it is concluded that mediation is not possible (Kenny 2013). However, there are differences in opinion.

Steps 2 and 3 are essential in establishing mediation. James and Brett argue that Step 3 need not control for the causal variable. If there was complete mediation, then controlling for the causal variable is not necessary (James and Brett 1984). As complete mediation does not always take place, controlling for variable X in Step 3 is advised.

8.4 **Results**

Between September 2008 and September 2011, 1437 participants were recruited; 14 were ineligible following their baseline visit and 1 participant withdrew consent for data to be used. The data from these individuals are excluded from subsequent analyses. See

Figure 17 for the study flow chart.

Characteristics of the cohort

There were 1432 participants included in these analyses (Table 23). The mean age of the sample was 60 years (±11.06), 54% were male and 51%, 38.1% and 11% were of white, black and South Asian / other ethnicities respectively. In the cohort, 35% of participants had managerial, administrative and professional occupations, 10% had intermediate occupations, 11% were small employers or own account workers, 14% had lower supervisory and technical occupations and 22% worked in semi-routine and routine occupations.

At baseline the majority of the cohort (78.6%) lived in deprived areas where mean levels of violent crime (per LSOA) were 3.5 (±3.03) incidents per month. The mean number of police in each ward was 5.1 (±1.48). Most individuals had favourable perceptions of their neighbourhood (58.5%). Around 70% of participants lived within

300 metres of green space and within 360 metres of a recreational facility. The mean number of fast food outlets within a 400 metre radius from residential address was 5.8 (±4.94). Participants reported eating healthy 4.9 (±1.64) days of the week and engaging in at least 30 minutes of physical activity on 2.6 (±2.16) days of the week. The median HbA1c was 48.6 mmol/mol (IQR = 43.17 – 48.63).

Table 23 Baseline characteristics of the sample (n = 1432)

Variable	Total (n (%) / mean (SD)
Age (years)	56.0 (11.06)
Gender	785 (54.3%)
Ethnicity	
White	725 (50.6%)
Black	546 (38.1%)
South Asian / other	161 (11.2%)
NS-SEC	
1	508 (35.1%)
2	140 (9.7%)
3	165 (11.4%)
4	200 (13.8%)
5	316 (21.8%)
IMD	
Most deprived	1137 (78.6%)
Least deprived	293 (20.2%)
Violent crime	3.5 (3.03)
Total police	5.1 (1.48)
Perceptions of neighbourhood	
Least problems	846 (58.5%)
Most problems	525 (36.3%)
Recreational facilities	
<120m	174 (12.0%)
120 – 239m	410 (28.3%)
240 – 359m	401 (27.7%)
≥ 360m	445 (30.8%)
Green space	
<100m	217 (18.7%)
100 - 199m	361 (24.9%)
200 – 299m	280 (19.4%)
≥ 300m	518 (35.8%)
Density of fast food outlets	5.8 (4.94)
SDSCA healthy diet (days/week)	4.9 (1.64)
SDSCA Exercise (days/week)	2.6 (2.16)
Median HbA1c (mmol/mol)	48.6 (43.17 – 48.63)

IMD: Index of Multiple Deprivation; SDSCA: Summary of Diabetes Self-Care Activities; NS-SEC: National Statistics Socio-Economic Classification; m: metres; for categorical variables, data are presented as n(%) with the exception of HbA1c which is median (IQR). For continuous variables, data are presented as mean (SD); *Percentages may not add up to 100 due to missing data.

The correlation matrices of independent variables described in this chapter can be found in Table 24. Although variables are correlated, no variables were highly collinear which would limit the validity of findings of any one predictor. Most of the objective area level neighbourhood measures were associated with one another. However, subjective individual characteristics were only weakly associated with total numbers of police: favourable neighbourhood perceptions were associated with fewer police ($p < 0.05$).

Table 24 Correlation matrix of independent variables

	Violent Crime	Total Police	IMD	Density of fast food restaurants	Distance to recreational facilities	Distance to green space	Neighbourhood perceptions
Violent Crime	1.00						
Total Police	-0.02	1.00					
IMD	-0.37**	-0.07*	1.00				
Density of fast food restaurants	0.26**	-0.10**	0.19**	1.00			
Distance to recreational facilities	-0.08*	0.002	0.09*	-0.12**	1.00		
Distance to green space	-0.18**	0.21**	0.37**	-0.19**	0.19**	1.00	
Neighbourhood perceptions	-0.004	-0.06*	0.05	-0.03	0.007	-0.01	1.00

*<0.001; **<0.01; IMD: Index of Multiple Deprivation; NS-SEC: National Statistics Socio-Economic Classification; for neighbourhood perceptions, lower scores = more neighbourhood problems.

For the cohort, when accounting for clustering within GP, the only neighbourhood variable to be significantly associated with HbA1c at 2 years was total police numbers (b = -0;63; CI = -1.19, -0.08) (

Variable	Unadjusted [a^]		Unadjusted [^] (n = 830)		Adjusted (n = 830)*	
	b (95% CI)	p value	b (95% CI)	p value	b (95% CI)	p value
Constant					42.07	
Age	-0.25 (-0.33, -0.18)	<0.001	-0.26 (-0.34, -0.18)	<0.001	-0.16 (-0.24, -0.07)	<0.001
Gender						
Male	1		1		1	
Female	-0.98 (-2.60, 0.64)	0.24	-0.86 (-2.70, 0.98)	0.36	0.72 (-1.45, 2.11)	0.72

Ethnicity						
White			1		1	
Black	1.58 (-0.16, 3.33)	0.08	1.77 (-0.22, 3.77)	0.08	-0.01 (-1.97 1.95)	0.99
South Asian / other	1.80 (-0.87, 4.46)	0.19	1.64 (-1.36, 4.63)	0.29	-0.21 (-2.92, 2.49)	0.88
NS-SEC						
Managerial administrative or professional occupations	1		1		1	
Intermediate occupations	-0.072 (-3.55, 2.21)	0.62	-1.92 (-4.93, 1.09)	0.21	-2.24 (-5.01, 0.54)	0.11
Small employers and own account workers	-1.01 (-3.76, 1.73)	0.47	-0.53 (-3.40, 2.34)	0.71	-0.56 (-3.14, 2.02)	0.67
Lower supervisory and technical occupations	1.12 (-1.46, 3.70)	0.40	1.65 (-1.13, 4.43)	0.25	0.95 (-1.54, 3.43)	0.46
Semi-routine and routine occupations	0.18 (-2.09, 2.44)	0.88	0.26 (-2.17, 2.70)	0.83	-0.65 (-2.84, 1.53)	0.56
Neighbourhood perceptions						
Least problems	1		1		1	
Most problems	0.79 (-0.91, 2.49)	0.36	0.34 (-1.51, 2.20)	0.72	-0.10 (-1.83, 1.64)	0.91
IMD						
Most deprived	1		1		1	
Least deprived	-0.16 (-2.12, 1.81)	0.88	0.07 (-2.12, 2.26)	0.95	1.23(-0.97, 3.44)	0.27
Violent crime	0.02 (-0.25, 0.29)	0.86	-0.01 (-0.31, 0.29)	0.95	0.07 (-0.22, 0.35)	0.65
Total police	-0;63 (-1.19, -0.08)	0.03	-0.61 (-1.23, 0.01)	0.05	-0.13 (-0.72, 0.35)	0.66
Green space						
<100m	1		1		1	
100 - 199m	0.54 (-1.92, 3.01)	0.67	-0.11 (-2.92, 2.70)	0.94	0.15 (-2.35, 2.65)	0.91
200 – 299m	-1.36 (-3.98, 1.26)	0.31	-2.19 (-5.19, 0.81)	0.15	-1.42 (-4.10, 1.26)	0.30
≥ 300m	-1.46 (-3.76, 0.85)	0.22	-1.80 (-4.43, 0.82)	0.18	-1.44 (-3.96, 1.07)	0.26
Recreational facilities						
<120m	1		1		1	
120 – 239m	2.07 (-0.69, 4.83)	0.14	1.25 (-1.87, 4.37)	0.43	0.05 (-2.71, 2.81)	0.97
240 – 359m	2.80 (0.03, 5.57)	0.05	2.39 (-0.73, 5.51)	0.13	1.70 (-1.05, 4.46)	0.23
≥ 360m	1.25 (-1.51, 4.00)	0.37	0.90 (-2.20, 4.00)	0.57	0.98 (-1.81, 3.76)	0.49
Fast food outlets	-0.04 (-0.21, 0.12)	0.63	-0.08 (-0.27, 0.11)	0.41	-0.12 (-0.29, 0.06)	0.19
Depression status						
Not depressed	1		1		1	
Depressed	2.70 (0.39, 5.01)	0.02	2.91 (0.12, 5.59)	0.03	1.13 (-1.30, 3.57)	0.36
Diabetes medication						
No	1		1		1	
Yes	6.95 (5.30, 8.60)	<0.001	7.25 (5.38, 9.12)	<0.001	2.12 (0.25, 4.00)	0.03
Baseline HbA1c (mmol/mol)	0.34 (0.30, 0.40)	<0.001	0.40 (0.34, 0.45)	<0.001	0.35 (0.29, 0.41)	<0.001
Any macro						
No	1		1		1	
Yes	-1.71 (-4.48, 1.06)	0.23	-1.81 (-4.82, 1.19)	0.24	-1.18 (-3.92, 1.57)	0.40

Table 25). Higher numbers of police were associated with lower HbA1c. Similar results were found when conducting the same analysis with the restricted sample used in adjusted analyses. In adjusted analyses, when controlling for age, gender, ethnicity, individual socio-economic status, depression status, antidiabetic medication, baseline HbA1c and macrovascular events, there were no significant associations between neighbourhood factors and HbA1c at 2 years. The ICC was 0.75% in this model.

Variable	Unadjusted [a^]	Unadjusted [^] (n = 830)	Adjusted (n = 830)*

	b (95% CI)	p value	b (95% CI)	p value	b (95% CI)	p value
Constant					42.07	
Age	-0.25 (-0.33, -0.18)	<0.001	-0.26 (-0.34, -0.18)	<0.001	-0.16 (-0.24, -0.07)	<0.001
Gender						
Male	1		1		1	
Female	-0.98 (-2.60, 0.64)	0.24	-0.86 (-2.70, 0.98)	0.36	0.72 (-1.45, 2.11)	0.72
Ethnicity						
White			1		1	
Black	1.58 (-0.16, 3.33)	0.08	1.77 (-0.22, 3.77)	0.08	-0.01 (-1.97 1.95)	0.99
South Asian / other	1.80 (-0.87, 4.46)	0.19	1.64 (-1.36, 4.63)	0.29	-0.21 (-2.92, 2.49)	0.88
NS-SEC						
Managerial administrative or professional occupations	1		1		1	
Intermediate occupations	-0.072 (-3.55, 2.21)	0.62	-1.92 (-4.93, 1.09)	0.21	-2.24 (-5.01, 0.54)	0.11
Small employers and own account workers	-1.01 (-3.76, 1.73)	0.47	-0.53 (-3.40, 2.34)	0.71	-0.56 (-3.14, 2.02)	0.67
Lower supervisory and technical occupations	1.12 (-1.46, 3.70)	0.40	1.65 (-1.13, 4.43)	0.25	0.95 (-1.54, 3.43)	0.46
Semi-routine and routine occupations	0.18 (-2.09, 2.44)	0.88	0.26 (-2.17, 2.70)	0.83	-0.65 (-2.84, 1.53)	0.56
Neighbourhood perceptions						
Least problems	1		1		1	
Most problems	0.79 (-0.91, 2.49)	0.36	0.34 (-1.51, 2.20)	0.72	-0.10 (-1.83, 1.64)	0.91
IMD						
Most deprived	1		1		1	
Least deprived	-0.16 (-2.12, 1.81)	0.88	0.07 (-2.12, 2.26)	0.95	1.23(-0.97, 3.44)	0.27
Violent crime	0.02 (-0.25, 0.29)	0.86	-0.01 (-0.31, 0.29)	0.95	0.07 (-0.22, 0.35)	0.65
Total police	-0;63 (-1.19, -0.08)	0.03	-0.61 (-1.23, 0.01)	0.05	-0.13 (-0.72, 0.35)	0.66
Green space						
<100m	1		1		1	
100 - 199m	0.54 (-1.92, 3.01)	0.67	-0.11 (-2.92, 2.70)	0.94	0.15 (-2.35, 2.65)	0.91
200 – 299m	-1.36 (-3.98, 1.26)	0.31	-2.19 (-5.19, 0.81)	0.15	-1.42 (-4.10, 1.26)	0.30
≥ 300m	-1.46 (-3.76, 0.85)	0.22	-1.80 (-4.43, 0.82)	0.18	-1.44 (-3.96, 1.07)	0.26
Recreational facilities						
<120m	1		1		1	
120 – 239m	2.07 (-0.69, 4.83)	0.14	1.25 (-1.87, 4.37)	0.43	0.05 (-2.71, 2.81)	0.97
240 – 359m	2.80 (0.03, 5.57)	0.05	2.39 (-0.73, 5.51)	0.13	1.70 (-1.05, 4.46)	0.23
≥ 360m	1.25 (-1.51, 4.00)	0.37	0.90 (-2.20, 4.00)	0.57	0.98 (-1.81, 3.76)	0.49
Fast food outlets	-0.04 (-0.21, 0.12)	0.63	-0.08 (-0.27, 0.11)	0.41	-0.12 (-0.29, 0.06)	0.19
Depression status						
Not depressed	1		1		1	
Depressed	2.70 (0.39, 5.01)	0.02	2.91 (0.12, 5.59)	0.03	1.13 (-1.30, 3.57)	0.36
Diabetes medication						
No	1		1		1	
Yes	6.95 (5.30, 8.60)	<0.001	7.25 (5.38, 9.12)	<0.001	2.12 (0.25, 4.00)	0.03
Baseline HbA1c (mmol/mol)	0.34 (0.30, 0.40)	<0.001	0.40 (0.34, 0.45)	<0.001	0.35 (0.29, 0.41)	<0.001
Any macro						
No	1		1		1	
Yes	-1.71 (-4.48, 1.06)	0.23	-1.81 (-4.82, 1.19)	0.24	-1.18 (-3.92, 1.57)	0.40

Table 25 Unadjusted and adjusted analyses of the association between neighbourhood variables and HbA1c at 2 years

[a] Analyses using all cases for whom data were available, n is variable; ^Unadjusted analyses accounting for clustering within GP only; *Adjusted analyses also accounted for clustering within GP; comparisons are made against reference group (1st listed group). CI: Confidence Interval; IMD: Index of Multiple Deprivation; NS-SEC: National Statistics Socio-Economic Classification; m: metres.

Mediational analyses

In the case of significant associations between neighbourhood variables and HbA1c, the occurrence of mediation was explored. As total police numbers were associated with HbA1c it was of interest to determine whether lifestyle factors (diet and exercise) mediate this association. These analyses were performed in 4 steps as outlined by Baron and Kenny (1986).

Step 1

Demonstrate that the independent variable (total police) is associated with the dependent variable (HbA1c).

This stage establishes that there is an association that might be mediated. Total police was not significantly associated with HbA1c (b = -0.13; CI = -0.72, 0.35)). The assumptions in stages 1 – 3 must all be met for mediation to take place. As the assumption in Step 1 was not met it can be concluded that there is no mediation present.

The assumptions in stages 1 – 3 must all be met. The assumption is Step 1 was not. Because of this it is concluded there is no mediation.

8.5 **Discussion**

This study aimed to investigate the association between the social neighbourhood environment and HbA1c over 2 years. In this inner-city, multi-ethnic cohort with newly diagnosed type 2 diabetes, neighbourhood factors were not independently associated with glycaemic control.

Although few studies have considered the effect of the social neighbourhood environment on diabetes outcomes, the results of the present study are at odds with the limited body of existing research (Geraghty et al. 2010, Laraia et al. 2012). The

explanations for the lack of associations in this thesis will be discussed in three sections: i) deprivation, crime and policing), ii) the obesogenic environment and iii) individual neighbourhood perceptions.

8.5.viii Deprivation, crime and policing

The neighbourhood environment may not be an important construct for individuals with type 2 diabetes and may, rather, contribute to the development of the disease. Area level deprivation is a risk factor for insulin resistance and type 2 diabetes (Cox et al. 2007, Diez Roux et al. 2002). The neighbourhood may therefore better explain the social patterning of the disease rather than variations in self-management in people with diabetes. The newly diagnosed diabetes status may also account for the lack of association. Two studies that do report an association between deprivation and poor glycaemic control in type 2 diabetes (Laraia et al. 2012, Geraghty et al. 2010) report significantly higher mean HbA1c values at baseline for their participants when compared to the SOUL-D cohort indicating that these studies recruited established diabetes populations (duration of diabetes is not reported). The mean HbA1c in the DISTANCE study was 58.5 mmol/mol and 13.4% of the sample had an HbA1c of ≥74.9 mmol/mol (Laraia et al. 2012) and Geraghty and colleagues (2010) report the mean HbA1c of their participants to be 55.8 mmol/mol. The relatively young newly diagnosed cohort who have adequate HbA1c at year 2 with few diabetes complications (Winkley et al. 2013) may not be reliant on, or influenced by, their proximal neighbourhood or perceive it as bad.

Another possible explanation for the lack of association is that SOUL-D recruited from health 'resilient' neighbourhoods. The SOUL-D cohort would therefore display better health outcomes than would be predicted given their deprivation status (Doran et al. 2006). Certain areas in South East London, including those in the setting of SOUL-D, have been previously identified as a minority of health resilient areas (these areas include the deprived parliamentary constituencies of North Southwark, Bermondsey,

Peckham, Vauxhall and Camberwell) (Tunstall et al. 2007, Cairns et al. 2012). These overachieving neighbourhoods are characterised by large ethnic minority populations, high levels of unemployment, overcrowding, rented housing and lone parenthood (Cairns et al. 2012), similar findings are reported in New Zealand (Pearson et al. 2013). These characteristics are comparable to the SOUL-D cohort which was recruited from multi-ethnic, densely populated, deprived urban areas.

The ethnically diverse nature of South East London may also be protective to the potentially harmful effect of the neighbourhood environment. The 'ethnic density effect' purports that higher concentrations of one's own ethnic group may have positive effects on health (Halpern and Nazroo 2000) through good social support, a sense of community and a reduction in adverse experience such as hostility or racism (Bécares et al. 2009, Whitley et al. 2006). Due to these factors, the concentration of minority ethnic groups in the SOUL-D cohort may protect against the potentially harmful effects of adverse neighbourhood conditions. An additional consideration is that the cohort consisted of some of the most deprived local authorities in the UK. Approximately 60% of SOUL-D participants live within 25% of the most deprived neighbourhoods in the UK. The lack of variation in deprivation scores may have been too small to observe any differences in associations with HbA1c. The three boroughs are also ranked within the top eight least peaceful local authority areas in the UK, where 'peacefulness' is a composite measure of homicide, violent crime, weapons crime, public disorder and police data (The Institute for Economics and Peace 2013). This again indicates that the SOUL-D sampling frame is similar, with a lack of variation in neighbourhood environments.

8.5.ix The obesogenic environment

The obesogenic environment was not associated with glycaemic control in the present study. The SOUL-D sampling frame is 'resource rich' with little variation in access to resources. South East London, in general, is highly commercialised with densely located local amenities despite significant levels of deprivation. For example, the mean number of fast food outlets in the SOUL-D boroughs is: Lambeth = 329, Lewisham = 351 and Southwark = 232, significantly higher than the national average where the mean number of outlets is 140 (Public Health England 2012). A similar pattern is observed with access to recreational facilities and green space. The majority of individuals lived within 300 metres of green space and within 360 metres of a recreational facility. Compared to other research using similar measures, our study demonstrated better access to these resources. This consequently led to clustered independent variables with small ranges. As a comparison, a study by Coombes et al. (2010) reported that 55% of their sample lived within 300m of green space, this is compared to 68% in the present study. The composition of inner city London may be atypical of inner city locations for a number of reasons; i) the allocation of resources; ii) population density; iii) ethnic density and iv) hypothesised atypical social patterning, where immense wealth sits alongside very deprived areas. The measures used in this thesis might be more applicable to larger study areas, smaller cities or countryside locations where greater variation in deprivation and access to resources exists.

Previously, the majority of research has taken place in the US. Here, evidence advocates a larger role of the obesogenic environment than in UK studies. It is probably not the case that the food environment is only important in the US, but rather that the processes explaining geographical variances in obesity levels may be different. Geographical differences may result from macro – level processes for example social, cultural, economic and regulatory factors which govern the provision, purchase and consumption of food. These factors may differ considerably between

countries (Cummins and Macintyre 2006). From a social perspective, the normalisation of obesity may be an important contributing factor which is further encouraged by the 'toxic food culture' evident in the US, more so than any other country, where 'to supersize' has become a verb, costs only a few cents and 'fast food advertisements saturate the airwaves' (Muray 2001).

8.5.x Individual level perceptions of the neighbourhood environment

Our finding adds to expanding literature on the simultaneous study of objective and subjective measures. In the present study, in contrast to findings in the general population (Ellaway et al. 2001, Wilson et al. 2004), neighbourhood problems were not associated with glycaemic control. Regardless of objective deprivation and access to local resources, if a resident does not perceive their local area as deprived, then it may not have a negative effect on health outcomes. The majority of participants in SOUL-D did not report problems in their neighbourhood. Three possible reasons for this finding are that i) South East London is a desirable location with good access to amenities and very good transport links, ii) social acceptability bias led participants to report that they lived in a desirable area and iii) this question did not accurately measure neighbourhood problems. These reasons may explain the lack of association between neighbourhood perceptions and glycaemic control.

At the time of writing, this is the first prospective study of the association between the neighbourhood environment and glycaemic control in type 2 diabetes. Strengths of the study include its longitudinal design, population-based approach and the comprehensive assessment of the neighbourhood environment at an individual and area level which included both objective and subjective measures. The use of GIS is another strength, which allowed for the measurement of distances along the road network with accuracy. Other studies utilising GIS have used Euclidian distance which does not always reflect actual distance.

However there are limitations, these largely relate to methodological concerns already described in the neighbourhood and health literature. The present study used administratively defined boundaries as proxies for neighbourhoods, primarily at LSOA, but also ward level. There is little consensus which spatial area is most relevant to health. Definitions of neighbourhoods have varied between 400m to 8km from residential address (Papas et al. 2007) and even more abstract definitions such as 'within a 5 minute drive' exist (Giles-Corti and Donovan 2002). Furthermore, administratively defined areas may not be consistent with how a resident defines their neighbourhood (Huie 2001). For example, an individual reliant on public transport may report having a smaller neighbourhood environment than an individual who owns a car and others define their neighbourhood in terms of proximity to social contacts (Guest and Lee 1984).

This study did not consider subjective assessments of the quality of green space or recreational facilities. This may have been an important omission as factors such as perceived safety and aesthetic quality of green space influence its use. It also did not take into account the cost of recreational facilities which may be an important confounder, particularly in the relatively deprived setting. The size of green space was also not considered, green space was included in analyses regardless of size. There may be some green spaces that are too small and unsuitable for physical activity. Also, these analyses were based exclusively on residential address. There was no information about the availability of recreational facilities or green space around work locations where people may shop and engage in physical activity.

Neighbourhoods are not static features, but change over time in response to cultural, economic and societal factors. These changes may have made it difficult to estimate the effects of the neighbourhood environment on HbA1c, as data were only used from one time point. However, our cohort appears to be relatively stable. Only 8.5% of individuals had moved in the 2 years following the baseline assessment, and most individuals moved within the same borough of South East London. Generally, inner

London has a very mobile and transient population who move both nationally and internationally. The relative stability of SOUL-D may suggest that a diagnosis of type 2 diabetes makes moving less likely, possibly due to the importance of access to healthcare.

This thesis did not consider other outcomes associated with environmental stressors such as cardiovascular disease, cortisol and C-reactive protein (CRP) levels. In this newly diagnosed sample, most of who were identified early on in the disease (demonstrated by relatively low HbA1c levels) there may be a lag time in which the neighbourhood environment influences HbA1c. Markers of cardiovascular disease, cortisol or CRP levels may have been susceptible to the influence of the neighbourhood environment for a longer period of time making an association between neighbourhood variables and these outcomes more likely. An association with HbA1c may be observed with a longer follow-up period.

8.6 **Conclusion**

Consistent evidence reports that health is spatially patterned but the present study suggests that where people live within an urban community of South London does not affect glycaemic control in those with newly diagnosed type 2 diabetes. However, this may be a result of the 'London-effect' or the short follow-up period. Given the limitations, policy makers should not ignore the effect of the neighbourhood environment on health outcomes. Consistent findings in the general health literature, most notably obesity and cardiovascular risk, underscore the importance of understanding how individuals interact with their environments in order to establish the possibility of large scale environmental interventions.

Chapter 9 Discussion

9.1 **Synopsis**

Social factors have prognostic significance for biomedical outcomes, morbidity and mortality across a range of conditions but the evidence base for these associations in type 2 diabetes is limited. This thesis investigated the association between social factors and glycaemic control using a theoretical model informed by epidemiological principles which was introduced in Chapter 1. Testing this model in a prospective cohort study of newly diagnosed type 2 diabetes, by applying a range of statistical techniques, there was no consistent evidence for a role of social factors in glycaemic control at the individual or area level. The results are discussed in terms of the limitations of the methods and possible explanations for the lack of associations are proposed. The contribution of these findings to existing literature and their clinical implications are also suggested.

9.2 **Summary of key findings**

This was a prospective cohort study of newly diagnosed type 2 diabetes in 3 multi-ethnic and socio-economically diverse boroughs of South East London. It aimed to explore the social determinants of glycaemic control using 2 social dimensions, or 'layers', theoretically conceptualised in the Dahlgren and Whitehead (2007) model: social support and the neighbourhood environment.

Social factors are important variables with prognostic significance for mental and physical health and are drivers of health inequity (Marmot 2005). However, whether they have a causal effect on glycaemic control in type 2 diabetes is inconclusive. Chapter 1 described the setting of this thesis. It documented the rising prevalence of type 2 diabetes, its epidemiology, management and the potentially important role for social factors. It also introduced the social determinants of health and proposed a testable epidemiological multi-level model for use in this thesis (Figure 6).

Chapter 2 synthesised the social support literature. Social support is associated with morbidity and mortality and is considered a risk factor on a scale equivalent to smoking or obesity in epidemiological studies (Holt-Lunstad et al. 2010). This association may be modified by population sub-groups, gender, ethnicity or depression status. In type 2 diabetes, there was face validity for examining whether social support, in the form of assistance from friends and family members, may be an important resource in the successful management of the disease, for example, when making lifestyle changes and adhering to professional advice, but evidence remains inconclusive. A systematic review of the association between informal sources of social support and glycaemic control in adults with type 2 diabetes was conducted (Chapter 3) (Stopford et al. 2013). It found that only family support and multidimensional assessments of social support were associated with HbA1c. However, the review

identified methodological issues: these included marked variation in study populations, setting, measurement of social support and definition of HbA1c.

Chapter 4 summarised the evidence for an important role of the neighbourhood, at an individual and area level, in the management of type 2 diabetes. The neighbourhood environment is associated with morbidity, mortality, risk of chronic disease and healthy lifestyle behaviours, primarily in obesity and cardiovascular disease. In a small number of studies, area level deprivation was associated with insulin resistance, type 2 diabetes and poor glycaemic control (Cox et al. 2007, Diez Roux et al. 2002, Laraia et al. 2012, Geraghty et al. 2010), however these were cross-sectional and used populations with established diabetes. The review found that no studies have prospectively investigated the association between other features of the neighbourhood environment and HbA1c in people with newly diagnosed type 2 diabetes.

This thesis is embedded within the SOUL-D study, a prospective cohort of 1447 individuals with newly diagnosed type 2 diabetes. The setting was primary care centres across 3 South London boroughs, representing a multi-ethnic and socio-economically diverse population. Demographic, biological, social and psychological data were collected using standardised clinical assessments and medical records review. The main outcome was HbA1c at 2 years. Mixed-effects multi-level models were used to determine the associations between explanatory social variables and HbA1c when accounting for clustering within GPs. Analyses were stratified where necessary, based on existing theory. The specific hypotheses and the findings will be summarised and discussed below.

Chapter 6 described the baseline characteristics of the SOUL-D sample and compared these to existing cohorts. From 96 general practices, 1447 participants were recruited between September 2008 and November 2011. Their mean age was 56 years (±11.06), 55% were male and 51%, 38% and 11% of the sample were white, black and south

Asian/ other ethnicities respectively. The mean BMI was 31.9 kg/m^2 (± 6.50) and the median HbA1c was 48.6 mmol/mol (IQR = 43.17 – 48.63). When compared to other cohorts it appears the characteristics of people being diagnosed with type 2 diabetes are changing. More recent cohorts (SOUL-D included) reported younger age at diagnosis and higher BMI reflecting the effects of screening programmes in primary care and the higher prevalence of obesity. The ethnic composition of SOUL-D was also notably different to existing cohorts; 51% of the SOUL-D participants were white, compared to 86% in UKPDS and 93-97% in other cohorts. This finding demonstrated two important points: i) the increased prevalence of diabetes in individuals of black and South Asian ethnicity and ii) in contrast to existing theories, the willingness of people from all ethnic groups to participate in research.

In Chapter 7, the hypotheses that increased i) functional and ii) structural social support were associated with decreased HbA1c were rejected. Social support was not associated with HbA1c in individuals with newly diagnosed type 2 diabetes. However, there is tentative evidence to support the third hypothesis, that the association between social support and HbA1c varies according to demographic group (gender, ethnicity and depression status), although associations were not significant.

In Chapter 8 neighbourhood factors were not associated with HbA1c at 2 years, except for total police numbers which were inversely associated with HbA1c. A mediating effect of diet and exercise was also tested to explain any associations but there was no evidence to support any mediation.

9.3 **Limitation of methods**

As with any epidemiological study, the interpretation and evaluation of the validity of the findings require consideration of whether associations between exposures and

outcomes are due to alternative explanations such as i) the role of bias, ii) the role of chance and iii) confounding. Even though the present study did not report any significant statistical associations, it is still important to explore the reliability and the validity of the non-significance.

9.3.i The role of bias

The association between an exposure and outcome may be explained by the role of bias. Bias is a systematic error which can be introduced by i) selection bias; ii) loss to follow and iii) information bias.

Selection bias may occur when the inclusion of cases into the study are associated with the outcome of interest (Hennekens and Buring 1987). This study used a prospective cohort design, which reduces the possibility of selection bias by caseness. As previously described, this type of bias is more of a concern in case-control or retrospective cohort designs (Hennekens and Buring 1987). Strengths of SOUL-D are that it is largely representative in terms of ethnicity and socio-economic status and that only 32% of invited individuals did not take part. However, there was a population of individuals excluded from the SOUL-D cohort who are more likely to have worse biomedical outcomes. This included individuals who were housebound and therefore not able to visit the GP, individuals who had severe mental illness and individuals who were not fluent in English. Those who were housebound may be more reliant on social support and their exclusion may have led to an underestimation of the association between social support and glycaemic control, and likewise for the other two exclusion criteria.

Attrition bias can occur if participant attrition is not representative of the study sample. This is almost inevitable with longitudinal designs. In this thesis, those who were lost to follow-up were younger, more likely to be female, black, less likely to be retired and more likely to be depressed. These characteristics are partially consistent

with previous research which reports attrition to be associated with older age, cognitive impairment, lower socio-economic status, mental health and longer follow-up. The attrition of younger individuals and people of black ethnicity may reflect the mobile and transient population of South East London. Younger people may be more likely to relocate and black participants frequently travelled abroad, usually to their country of origin, for long periods of time each year (ONS 2008). What is inconsistent is the association between attrition and gender. The present study reported more females lost to follow-up however other large studies, such as the Whitehall II study, reported more males lost to follow-up (Mein et al. 2012). The greater attrition of females may reflect the multiple active roles of females in the cohort: mother, spouse, grandmother, carer, alongside the demands and time constraints of employment.

Information bias results from wrong or inaccurate recording of data. With continuous variables, such as BMI, this is known as measurement error and with categorical variables such as disease status, it is referred to as misclassification. These types of bias may result from inaccuracy by researchers or by poor quality measures or their measurement. Three typical sources of information bias include i) questions about events in the past for which answers are often imprecise. In this study, information was verified with medical records where possible; ii) the way a researcher treats a participant during interview may determine how much detail and accuracy is put into responses and iii) human error in measurements, for example, when measuring height or weight, values may differ by researcher and by the equipment used. To keep this type of bias to a minimum, research assistants were trained, followed a standardized data collection schedule, used (where possible) the same equipment and data collection was checked.

Information bias may also arise from the use of self-report measures and the modification of answers in order to appear more socially desirable. This can manifest in 3 ways: i) incorrect reporting of information, ii) omitting information and iii) altering the magnitude of reported information, that is, over-reporting desirable behaviours

(e.g. medication adherence) and under-reporting undesirable ones (e.g. smoking). This type of bias is more common in face-to-face and telephone research than in postal surveys (Presser and Stinson 1998). Most pertinent to SOUL-D, individuals may have reported inflated levels of social support and more favourable perceptions of their neighbourhood. Methods such as anonymity and the assurance of confidentiality exist to reduce this problem however it is almost impossible to eliminate entirely. This type of bias can lead to false findings or obscure the existence of a true association, thus questioning the validity of results (Fadnes et al. 2009).

9.3.ii The role of confounding

Confounding variables are independent factors which are associated with the exposure and, independent of that exposure, the outcome of interest. The evaluation of confounding is critical to the interpretation of findings from epidemiological studies, in particular observational studies. Uncontrolled confounding is a significant concern to validity. In the present study, variables that were clinically or theoretically relevant were used as confounders. Stratification was another method used to correct for confounding, however, these techniques only allow for the control of variables that have been measured. Residual confounding refers to the distortion that remains after controlling for relevant confounding in both the design and analyses. There are 3 main causes:

i. There are additional variables which may act as confounders, but as no data were collected on these variables no attempt could be made to control for their effects. In social research, the possibility of residual confounding by individual level variables is a limitation and there is a lack of consensus regarding key cofounders. With the SOUL-D population in mind, these factors may include: culture; the perceived stigma of diagnosis; adherence to medication regimen; and health literacy. Furthermore, social factors are not discrete; they are overlapping and consequently are often collinear. This was important to consider in analyses; the number of social variables and confounders was kept

to a minimum and their inclusions were theoretically informed to cover a broad assessment of social support and the neighbourhood.

ii. Even in adjusted or stratified analyses, residual confounding may still be present if data on the confounding variables were not accurate. For example, if continuous or categorical data were collapsed into too few or crude groups. In this thesis, continuous variables were collapsed into groups for the purpose of analyses, however groups were determined based on statistical assumptions. For example where the ceiling effect occurred, groups were utilised to make the best use of data available.

iii. Measurement error when measuring confounding reduces the ability to adequately control for confounding variables. Efforts were made to train research assistants in the delivery of standardised data collection schedules.

9.3.iii The role of chance

If the study results cannot be explained by bias or confounding, then the role of chance must be considered as an alternative explanation. Observational studies are particularly susceptible to spurious findings as a large number of variables are collected and large sample sizes often create an impression of sufficient statistical power.

The P value, the probability of observing a test statistic as extreme, or more extreme, than the one that was observed, was 5%. This equals the probability of Type I error. When $p<0.05$, the null hypothesis was rejected and when $p>0.05$, the null hypothesis was accepted. When using the 5% level, there is a chance that 1 in 20 statistical tests will be false positives, that the null hypothesis was incorrectly rejected. Type II error occurs when the null hypothesis is incorrectly accepted. To reduce the probability of a

Type I error, a lower significance level could be used, but this increases the probability of a Type II error.

Three methods were used to mitigate the problems of chance. Firstly, this study had adequate power to detect an association. The reduced sample size used in multivariable analyses fell marginally short of the chosen sample size calculation but the sample used in these analyses still met the assumptions of Option 1 (n = 572) (alpha of 0.01, 90% power and a conservative explained variance of 5%) (Table 4). Although the sample size was based on variance explained, rather than effects of specific exposures, the sample size calculation did account for the inclusion of covariates and for the effect of clustering within GP.. Secondly, analyses were corrected for multiple comparisons. Hochberg's improved Bonferroni Method (Hochberg 1988) was used in Chapter 7 and 8 (Hochberg's procedure is more powerful than other multiple testing correction methods). Thirdly,formal tests of interactionwere used in stratified analyses in Chapter 7.

Alternatively, to reduce the risk of chance findings, the number of tests could have been reduced. However, this would have led to reduced number of hypotheses. Reducing the number of variables entered into the multivariable regression may have been inappropriate as in a multi-dimensional topic such as social support, this would risk missing an association if only a few concepts of social support were examined. Therefore, although there was no evidence for social determinants of glycaemic control I can be confident that the results are not sporadic or random.

9.4 **Alternative explanations of findings**

Assuming that the results of this thesis are unlikely to be explained by the role of bias, confounding or chance, it is important to consider alternative explanations for the

findings which did not provide evidence to support the epidemiological model presented in this thesis. These findings are in contrast to the wider social determinants of health literature which reports a consistent association between social factors and health outcomes. However, they are consistent with the systematic review in Chapter 3 where only 41% of studies reported an association between social support and glycaemic control. Potential explanations for the lack of association between social factors and glycaemic control in type 2 diabetes are discussed in terms of i) factors associated with the SOUL-D cohort and ii) methodological issues.

The social determinants of health are extensively documented. However what works for whom and under which conditions remain unanswered. The findings of this thesis may highlight an important subsection of the population for whom social factors are not important and social interventions may not be effective. Individuals with type 2 diabetes may represent a homogenous population where social determinants contribute to the onset, rather than the management, of the disease. The Accumulation of Risk model describes how factors that increase risk of disease gradually accumulate over the life course. With increasing numbers of risk factors there is increasing damage, and therefore malfunction, of biological systems. If this theory is applied to the SOUL-D population, an accumulation of risk factors may have led to the development of type 2 diabetes, which, by definition, makes SOUL-D a homogenous population. It would, therefore, only be with further accumulation or risk factors that variations in diabetes outcomes would be seen. It is known that poor social support and neighbourhood environments are risk factors for type 2 diabetes. When compared to the general population individuals with diagnosed type 2 diabetes have fewer social contacts and higher deprivation levels (Hempler et al. 2013, Aalto et al. 1996, Krishnan et al. 2010) so these factors may predispose rather than determine the course of the disease. However, interestingly, in the SOUL-D cohort this may not necessarily be the case. A larger proportion of SOUL-D were married, when compared to the general population (56.1% vs 48.2%), and fewer were single (24.5% vs 35.6%) (ONS 2011), although it must be acknowledged that the SOUL-D cohort had a higher mean age than the general population and statistics are therefore not directly

comparable. Social network data were normally distributed and reflects previous research in both diseased and general populations. These figures indicate that although the SOUL-D cohort may well be a homogenous population, they were not necessarily lacking in social support (measured by structural assessment of contacts).

The newly diagnosed nature of the cohort may be another explanation. The participants of SOUL-D may not have needed to draw on their social contacts or have been influenced by their neighbourhood environment. This may be for 2 reasons: Firstly, intensive medical management following a recent diagnosis. Patients will have contact with doctors, nurses, DESMOND educators, eye clinics and dieticians. There is a wealth of NHS support provided to individuals at the diagnosis of type 2 diabetes and t is possible that this support is so good it cannot be enhanced by informal sources of social support or by neighbourhood characteristics. Consequently, newly diagnosed individuals may rely on formal forms of social support from healthcare professionals, rather than drawing on informal sources. Secondly, the participants included in the SOUL-D study may have been a cohort of individuals with early good intentions and motivation for self-management at the diagnosis of a chronic disease. At the diagnosis people are informed about the optimal management of their condition and self-esteem may be high. It may take some time (perhaps longer than the 2 year follow up period in this study) before people realise i) the severity of their diagnosis and ii) that the management of a long term condition is multifaceted and challenging. People who did not view diabetes as a significant concern or who were less keenly interested in their health may represent a population of people that chose not participate in the study.

Thirdly, the SOUL-D sample was largely asymptomatic, with acceptable glycaemic control and few complications at diagnosis (Winkley et al. 2013). Participants may therefore have experienced few difficulties and not needed to utilise support resources or be restricted to rely on resources in their local area. Additionally, particularly at diagnosis, there may be a mismatch between the patient's idea of the disease and the information received by healthcare professionals due to the 'hidden'

nature of diabetes. Patients may not view themselves as 'sick' and therefore deem any suggested changes as unnecessary. Friends and family members may also face this problem. If family members are not aware of the requirements of type 2 diabetes, do not perceive them as significant, or, if they are overwhelmed by the multiple demands, appropriate support may not be given. This may be further compounded by the normalisation of obesity and associated disease, particularly in Western cultures. As such, the public perception of the disease may be nonchalant and inadvertently disregard the importance of healthy lifestyle behaviours and the debilitating nature of complications. Whether one lives in a neighbourhood conductive to healthy lifestyles is then irrelevant.

Stigma is an associated consideration which is increasingly reported in relation to type 2 diabetes. Recently, large studies have demonstrated that type 2 diabetes can be prevented, this highlights a role of individual behaviour and personal responsibility. With heightened media coverage and increasing awareness of type 2 diabetes in the general public, the perceptions of the disease are also changing. Anecdotally, these perceptions are less sympathetic to obesity and related disease and blame individuals for 'bringing it on themselves'. Consequently, those with type 2 diabetes may be reluctant to disclose their diagnosis for fear of being blamed, judged or discriminated against or out of a sense of shame or self-blame (Browne et al. 2013). Similar beliefs were elicited in qualitative research of 30 participants of the SOUL-D study who were interviewed about attendance of DESMOND (Winkley et al. 2014). A lack of information (i.e. not being informed about DESMOND) was described as the main reason for non-attendance but stigma was also a key theme. This study reported cultural, and often personal, beliefs that have not been previously described. This was overwhelmingly reported by Nigerian participants. Participants had not told their friends and family about their diagnosis and there were concerns surrounding the effect of diabetes on fertility and virility. These participants would therefore not attend DESMOND, which is delivered in a group format, for fear of members of their local community finding out about their diagnoses. Ethnicity has been previously cited as a factor associated with the non attendance of structured education programmes (Lucas

et al. 2013) however stigma and shame have not. The findings reported by Winkley and colleagues indicate that shame and stigma may be associated with certain ethnicities. As almost 50% of the SOUL-D cohort were of non-white ethnicity, it may have sampled a population who were less likely to inform friends and family about their diagnosis and therefore less able to elicit diabetes specific support. This theory is in line with the results of the SOUL-D study. For the most part, data indicated high levels of social support across the cohort, however, if participants had not told their family or friends about their diabetes they would not be able to discuss any worries surrounding their diagnosis or tap into the supportive resources. For this reason, participants may have 'carried on as normal' making no changes to lifestyle for fear of questioning. We therefore have a cohort with high levels of social support which, for many, has no impact on diabetes outcomes.

The importance of social determinants may only emerge with longer term follow-up when disease progression (progressive destruction of beta cells and worsening glycaemic control) leads to 'visible' complications (for example, deterioration in sight or ulcerations) and disability. If this is the case, we would expect to see the association between social variables and glycaemic control increase in strength over time. Complications of diabetes may elicit social support, or a different type of support from already supportive individuals. Complications and their associated impairment to daily function may also impose physical constraints and render people more reliant on local resources. At face value, these are logical explanations but our systematic review reported conflicting findings in established diabetes populations, the majority showing no association between social support variables and glycaemic control. However, there were significant methodological concerns which limit the validity of many of the included studies and the majority were cross-sectional. The measures included in this thesis were based on academic assumptions and given the consistent findings in the literature across a range of health conditions, there was no reason to believe that the social measures were either inaccurate or incorrect. It was assumed that social factors would be important in this population and it was acknowledged that social constructs are multifaceted and difficult to measure, so a range of social variables were included

to be as comprehensive as possible. But, whilst making considerable efforts to be methodologically correct, there remained no association. It must therefore be questioned whether the social measures used in this thesis were incorrect or whether they did not adequately assess social factors in this patient group.

This thesis echoes previous research in the social determinants literature where significant methodological challenges are frequently reported. Issues specifically relate to the definition, conceptualisation and measurement of social support and the neighbourhood (Stopford et al. 2013). This is further compounded by the measurement of heterogeneous social variables. Again, this was demonstrated in our systematic review (Chapter 3), where, out of 30 social support studies, 21 different assessments of social support were used (Stopford et al. 2013). Consequently, the reliability and validity of many social measures are not known.

The extensive '24-7' multiple self-management roles required in type 2 diabetes (diet, physical activity, self-monitoring, appointments, tablets and injects) may render the role of social factors more complex than in other conditions, where the main self-management role might be to administer medication at certain times of the day. Simply studying quantitative, uni-factorial dimensions of social constructs may be simplistic. This approach has been promoted in the neighbourhood literature as it allows for easy identification of important exposures but it ignores the complex, multifaceted and interlocking nature of one's social environs. As a result, we may be studying the wrong factors or failing to tap important latent constructs relevant to diabetes. On the other hand, multidimensional constructs of social variables homogenise broad and diverse dimensions and it becomes difficult to ascertain what a multidimensional tool is measuring and how to identify important variables. This is particularly pertinent to the social literature. Whilst multidimensional tools may allow for the measurement of 'latent constructs' it is very difficult to label, quantify and base subsequent interventions on poorly defined latent variables. As an example, a multidimensional construct such as 'diabetes self-management' is quite easily

measured using a composite questionnaire such as the Summary of Diabetes Self Care Activities (SDSCA). Although there will be associations between components of the questionnaire (diet, exercise, smoking, blood glucose testing and foot checks), each is well defined. This is significantly less easy to do with social variables and overlap between dimensions would be far greater. In the first instance, a qualitative approach would be helpful in order to i) establish the factors which patients themselves consider to be important in the management of type 2 diabetes and ii) ascertain the possibility of a more complex association between social determinants and glycaemic control.

It may be that a complex interaction between social factors did obscure any association. This may include a multifaceted interface between social network size, quality of relationship and perception of support. There also may be other social constructs particularly important to diabetes that need to be considered. Some examples may be i) reciprocity (social support may only be helpful if one feels that they can also provide assistance), ii) a sense of belonging (a feeling of personal involvement in a social group or relationship where the person feels that they play an integral role) or iii) shared beliefs or a common understanding (this may occur between a patient and doctor, or an individual with type 2 diabetes and their social network, where both parties acknowledge and agree on a course of action). There may also be an interface between social contacts and the neighbourhood environment. For example, individuals may be happier to walk further to attend a gym or buy healthier food if they are with a friend or neighbour. This could not have been captured with the measures used in this thesis. Consequently, a more complex analysis may be required when studying social factors in diabetes. With the progression of the literature and the development of multifaceted questionnaires, a weighted approach could always be adopted for analysis to reflect the most important constructs. Firstly, though, these constructs need to be identified.

The quality of social relationships and the quality of neighbourhood resources were not directly measured. An individual's perception of 'quality' may be more important

than mere existence of such features. When an individual indicates familial ties for example, no information is learnt about the closeness of the bond or the quality of the relationship. Quantitative scoring of social contacts makes the assumption that being married or having larger social networks results in support being provided but this may not be the case. For example, a hypothetical situation, a participant reports a large social network, scores highly on these measures and it is consequently assumed that he has good social support. But, on further questioning, this participant only talks to his mother when she needs assistance getting to the GP and talks to his brothers out of a sense of duty, he says good morning to the postman and attends church, but does not interact with other members. The likelihood is, that none of these individuals would be on 'stand-by' to provide support if it were needed. Similarly, consider an individual who is married but perceives low levels of social support. This individual is constantly being 'nagged' by their husband or wife but responds to this 'nagging'. The picture for this individual would also go against convention: the perception of low levels of social support (this individual may also report low quality social support) associated with optimal glycaemic control. Furthermore, the definition of high quality support may vary greatly between the patient, clinician or care-giver. From a patient's perspective, a relationship with a partner, for example, may be considered high quality if they are available to listen to concerns, provide reassurance, practical assistance and help with access to services. If this reassurance and access to services involves reinforcing existing lifestyles incompatible with adequate glycaemic control then the quality of the relationship remains high but to the detriment of glycaemic control. This same premise can be applied to the neighbourhood variables used in this thesis, the objective measures of green space and recreational disregarded the quality, reputation and price of resources, which are all important factors that influence the decision making process.

An additional methodological concern in the area level analyses relates to the definition and measurement of the neighbourhood. The preferred geographic area to which objective data could be matched was LSOA. This is the smallest administratively defined area in the UK which was used as a proxy for an individual's neighbourhood

and most reflective of the proximate area around a residential address. In a densely populated area such as South East London, the LSOA may not reflect what an individual perceives to be their neighbourhood. In South East London, immense wealth lives alongside deprivation. Deprivation indices for these two areas may be vastly different but may not have the expected gross impact on individuals living in these areas. An individual living in a 'deprived' area may perceive the neighbouring LSOA (which may be only metres away) to be their neighbourhood and therefore is not affected by the deprivation associated with their postcode. Thehe use of the term 'neighbourhood' may also incorrectly imply an independent and socially cohesive community but it should be remembered that individuals are not constrained to these areas, particularly in highly urbanised settings with good transport networks such as South East London. The LSOA level may be more relevant to a rural village setting. The definition of the neighbourhood may vary from person to person; for example, a less mobile individual may be reliant on a smaller geographical area and individuals who live near tube stations may be able to travel further than those reliant on the bus. Although it is a strength of this thesis that subjective and objective measures were used, in the setting of SOUL-D, the LSOA level may be too small. Super Output Areas (SOAs), or ward level (the level used for total police numbers) may therefore be most appropriate.

A further consideration is that advances in technology and modern media may be redefining how researchers should conceptualise social determinants. The internet has become an indispensable part of modern life serving an increasing proportion of social and domestic needs. This may be particularly true with social support, although additionally, the increasing use of the internet for shopping may render individuals less reliant on their neighbourhoods. Methods of communication such as e mail or instant messaging and virtual communities, such as Facebook and Twitter, are highly accessible and used by millions daily. Furthermore, specific supportive communities exist online for health related issues. There is a wealth of (un-moderated) discussion forums, within which people share experiences, ask questions, provide support and self-help but little is known about the role of such platforms in the social disparities of

health. These may be an important informal supportive resource for three reasons: i) the internet and Apps (computer software) can be accessed in any location at any time of the day meaning that, if needed, support is available 24 hours a day, 7 days a week ii) it may be easier to share concerns with a 'virtual' less personal source and iii) it is preferable not to be seen as a burden to friends and family and the internet provides an additional outlet. Measures used in this thesis did not include web based contacts or virtual social support and this may have been an important omission. Individuals using these platforms may have a large network of 'virtual supporters', and thus rely less on support from friends and family. On the questionnaires used in this thesis, these individuals would incorrectly resemble those with low levels of support. It is therefore necessary for the definition and measurement of social support to incorporate advances in technology.

9.5 How these findings add to existing research

The results from this thesis are important as they are at odds with previous research, particularly in relation to obesity and cardiovascular disease. However, this is one of the first prospective studies of social factors in people with type 2 diabetes, and it suggests that social factors may not be important in this population. This is significant from a public health perspective as it indicates that large scale social (population-based) interventions may not be equally helpful for all of society.

It may be concluded that there are groups of individuals for whom social factors do not play a significant role. As previously described, it is speculated that these populations include those who i) have type 2 diabetes, ii) are in frequent contact with primary care services, iii) have a recent diagnosis or iv) are relatively healthy with chronic conditions. These population characteristics have not been previously described and bring an additional dimension to existing literature which has generally made the assumption that social factors are important for the whole population.

An additional consideration is that this thesis found no evidence for a negative effect of social support such as nagging or harassment. This is in contrast to a small, but expanding, area of research that indicates a 'u shaped' effect of social support. This, again, may be a consequence of the characteristics of this population for example, friends and family members may not start nagging about the importance of self-care (eating healthily and exercise) until there are visible signs of illness or disability.

Rather than answering long-standing research questions in the social literature, this thesis unearthed further unanswered questions and reinforced existing methodological concerns.

9.6 **Clinical implications**

Although it is important for healthcare providers to consider the social contexts of their patients, at the time of diagnosis of type 2 diabetes, when receiving intensive medical management, social determinants may not be important. The conventional medical model at this time may be the most appropriate.

Despite this, there is an abundance of data that implicates an important role of social factors in the development of type 2 diabetes. Healthcare providers should therefore still make efforts to tailor clinical advice to their patients' needs particularly in terms of the social determinants of health, just as advice may be tailored to individuals who are housebound, for example. Understanding the extent to which an individual has access to supportive resources that may assist with medication regimen or an individuals' access to resources conductive to healthy lifestyles are two examples. Understanding these factors may improve patient understanding of advice, patient outcomes and reduce primary care and hospital attendance.

9.7 **Future research directions**

Although social factors were not significant predictors of HbA1c in this newly diagnosed population they are paradoxically exciting as the ongoing search for social mechanisms in diabetes may offer new insights into the understanding and management of the disease. Currently however, methodological inconsistencies are hampering the progression of the social determinants literature. Before mechanistic routes of action can be discussed or interventions can be designed, there are a number of factors to consider: i) developing epidemiological and testable theories on the social determinants of poor glycaemic control in type 2 diabetes, this may require a qualitative or mixed-methods approach; ii) improving the psychometric properties of measures to empirically test theories and developing 'gold standard' multi-dimensional assessment tools which are theoretically guided; iii) addressing reporting bias, residual confounding and reverse causation, issues particularly relevant to social research and iv) increasing and promoting the use of longitudinal research designs. One of the problems in this area of research is that there has been a tendency to proliferate an increasingly diverse and expanding set of risk factors, many lacking concrete evidence as to their effect on health. With many, it is unclear whether they are distinct from traditional and established risk factors. An indiscriminately expanding range of social risk factors poses problems for the future development of science, practice and policy regarding the role of social factors in health (House 2002). What is needed is to make a renewed effort to synthesize factors already known to be important contributors to health, and to place this evidence on firmer theoretical foundations.

Assuming that the findings in this thesis are valid and there is no association between social variables and glycaemic control in this population, it may be of primary importance to review the way we are thinking about the theoretical underpinnings of social factors. A deeper engagement in social theory may be needed at this point. Social epidemiology, as a discipline, has expanded rapidly over the last few decades. But because of this, much of social epidemiology is informed by theory that has been

'borrowed' from other disciplines and applied to the field (Galea and Link 2013). On the whole, social factors are not static constructs and vary in response to societal changes. The implication this holds is that theories in social epidemiology cannot be set in stone and theoretical foundations need to be revisited. As previously discussed, more recent technological developments such as social media, smart phone applications and online shopping may need to be incorporated into our conceptualisation of social theory and measurement of social factors. We may need to, temporarily, go back to the drawing board in this discipline.

Whilst doing so, the opportunity may be taken to find the best evidence surrounding social determinants using systematic reviews with advanced search strategies and where possible, meta analyses. This would help to inform the development of future research. Such scoping processes must take care not to favour certain study designs or methodologies and base the search for 'best evidence' on evidence derived from appropriate methodologies which answer each research question. This approach was highlighted in a report by the WHO following discussions about the relevance of the traditional hierarchy of evidence to social research.

It is not disputed that human beings are social animals. Our lives depend on other humans, we learn from other humans and we voluntarily choose to live alongside other humans. As such, we naturally congregate and provide support in times of crises, for example, natural disasters or terrorist attacks. The social ability of humans appears to be an innate response, indicating a human capacity for empathetic caring behaviour but how we can elicit and harvest this and use it advantageously in health research remains unknown, especially in the diabetes population. It has been suggested that before humans act in a social capacity, there must be a driving force or trigger. This implies that the characteristics or the supporter and the supportee, and the interaction between the two are important. Again, in order to meet this goal, theories on the social framework of society must be revisited.

With the current evidence base and gaps in our knowledge, it would not be helpful to attempt to design an intervention. The traditional hierarchy of evidence places meta-analyses and systematic reviews at the top, followed by RCTs and then cohort studies and case control studies. However, it is questionable whether this hierarchy is applicable to social research. This is for two reasons: i) the naturally occurring nature of social constructs is difficult to accurately artificially induce and therefore not appropriately evaluated in a RCT and ii) the range of questions that social research seeks to answer are much broader than the assessment of clinical effectiveness thus implicating the use of different designs. When studying social factors in interventions they lose their 'informal' nature and become 'formal'. This thesis deliberately did not measure formal forms of support as this contradicts the premise of utilising naturally occurring social factors as they are readily available, cheap and potentially modifiable resources which exist outside of healthcare settings. As a result, the optimal way to advance the study of informal, 'everyday' social factors in type 2 diabetes is to utilise a cohort with longer term follow-up. This would allow for the investigation of the effect of a range of social factors in established diabetes populations and in individuals with higher prevalence of complications and disability.

However, a first step may be to adopt a qualitative approach to guide theoretical redefinitions of social factors. It is important to establish how individuals with diabetes (both established and newly diagnosed) perceive social factors to influence their control of the disease. Due to the vast social literature, a qualitative approach may take place in 2 stages. The first stage may aim to gain a broad understanding of social factors and might have 3 main topic areas: i) factors that led to the development of type 2 diabetes, ii) factors that influence the management of type 2 diabetes (including any specific barriers) and iii) why these factors are important. This should aim to investigate the 'causes of the causes' of ill health. For example, if an individual describes a period of stress before the diagnosis of type 2 diabetes, it would be helpful to investigate the factors contributing to the stress as this may elicit social factors. The views and beliefs surrounding the influence of social factors will undoubtedly vary

between patient, healthcare professional and carer and it would be important to cover all perspectives.

The second stage would be a more in depth analysis based on the themes that emerged from stage 1. Taking social support as an example, it may focus on i) the most important providers of social support (formal or informal), ii) the qualities of these individuals (specific supportive behaviours and unhelpful forms of 'support') and iii) the benefit of social support in the management of type 2 diabetes. By conducting qualitative research, we will start to gain a better understanding about the constructs that should be quantitatively assessed. It would be of further interest to determine whether people are aware of the influence of the conditions into which we are born, grow, work, live and age. It may emerge that questions regarding ones social environs need to be accompanied by an explanation of their importance. Anecdotally, questions regarding ones social network and neighbourhood could easily be considered 'not relevant' or 'random' in medical research. A brief explanation surrounding their importance and their direct relevance to an individual may encourage thought in these questionnaires and avoid them being another obstacle in finishing a battery of questionnaires.

Having, perhaps, acquired a new understanding of the social determinants of health and new concepts to be measured, the next step would be to define variables and establish a way to measure those variables. Ideally, established questionnaires with good reliability and validity would be used, but these are difficult to come by in the social support and neighbourhood literature. So many social measures have good face validity but their measurement validity is questionable. A semi-structured assessment of social support might also be considered. This would allow a deeper, more comprehensive, exploration of social support. In the SOUL-D study, which was set up to investigate biological, psychological and social influences of glycaemic control, the length of each questionnaire was a concern. Consequently questionnaires that covered a range of constructs and were quick to administer were chosen. In a study set up

solely to investigate social variables more time would be available for their measurement. Ultimately, developing gold standard tools for use within social research will require a collaborative effort amongst researchers.

Another area of interest would be to investigate the existence of large datasets collecting social data. More specifically, large datasets of i) individuals with type 2 diabetes utilising different social variables to SOUL-D or ii) individuals with other long term conditions utilising similar social variables to SOUL-D. The former would allow us to establish whether there are other social variables that are associated with glycaemic control in people with type 2 diabetes and the latter would allow for the investigation of whether the findings of this thesis translate to individuals with other long term conditions, particularly those who are relatively healthy, at least in the medium term, and are without disability. Individuals eligible for the NHS Health Check Programme may be a potential cohort. The NHS Health Check Programme aims to prevent heart disease, stroke, diabetes, kidney disease and certain types of dementia. Once every 5 years, adults between the ages of 40 and 74 are invited to assess their risk in primary care. These individuals do not have a current diagnosis, and similarly to the SOUL-D cohort, may be asymptomatic. These individuals may also not perceive the need for help and would therefore not seek it. If findings replicate this thesis, it would suggest that social factors are only important at certain stages of the life and course of disease.

Although it may currently be premature, we should look to explore the possibility of text mining, the process of ascribing numerical indices to unstructured textual information. This is, most commonly, used for the analysis of unstructured open-ended responses from questionnaires but can also be used to filter out desirable terms or words. It would be of interest to investigate the acknowledgement and importance of social factors in medical records and referral letters for example. Text mining would allow such an approach. This would enable us to investigate the social factors that are most commonly reported which may highlight those which are seen as the largest barriers or those that pose the greatest problems for healthcare professionals and

their patients. Again, this approach may assist in the theoretical re-defining of social support in type 2 diabetes.

9.8 **Conclusions**

This was a prospective cohort study of individuals with newly diagnosed (< 6 months duration) type 2 diabetes. Participants were recruited from 3 multi-ethnic and socio-economically diverse boroughs of South East London. Social factors were not significant predictors of HbA1c in this newly diagnosed population. There are five possible explanations for this finding: i) social factors are not important for people with type 2 diabetes; ii) people with diabetes are a homogenous sub group of the population; iii) the newly diagnosed nature of the sample and relatively short follow-up period; iv) the social measures utilised did not measure the complex nature of social support or the neighbourhood and vi) advances in technology are changing the meaning of social determinants. In diabetes, current models of social factors appear to be insufficient. The diabetes epidemic indicates a need to revisit the theoretical underpinnings of the social dimension of type 2 diabetes which might be more complex than originally thought.

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Appendix I Social support and glycaemic control in type 2 diabetes: a systematic review of observational studies

Appendix II Eligibility checklist, information sheet and consent form

SOUL-D Study Screening Form

GP Surgery Name: **Search date: ……../……../……..**
Patient Practice ID Number:

PARTICIPANT ELIGIBILITY CHECKLIST
If NO to ANY question, stop screening here. Patient is ineligible for trial.

1. Diagnosis of T2DM ☐[0] No ☐[1] Yes

2. Maximum duration of T2DM ≤ 6 months ☐[0] No ☐[1] Yes

If yes, date of diagnosis: ……../……../……

3. Age (between 18 to 75 years) ☐[0] No ☐[1] Yes

TRIAL INCLUSION CRITERIA
If NO to ANY question, stop screening here. Patient is excluded from trial.

4. Fluent in English ☐[0] No ☐[1] Yes

5. GP/Resident in LSLB ☐[0] No ☐[1] Yes

TRIAL EXCLUSION CRITERIA
If YES to ANY question, stop screening here. Patient is excluded from trial.

6. Severe mental illness: ☐[0] No ☐[1] Yes
   - *Defined as: manic depression, psychosis, learning disability, dementia, severe personality disorder, schizophrenia*

7. Terminal illness ☐[0] No ☐[1] Yes
   If yes, list ……..

8. Temporary residents ☐[0] No ☐[1] Yes

9. Other types of diabetes ☐[0] No ☐[1] Yes

10. Severe diabetes complications ☐[0] No ☐[1] Yes
    - *Defined as: registered blind, kidney dialysis, above the knee amputation*

If ELIGIBLE for trial:

1. Date of Birth: ……/……../……
2. Gender: □[1] Male □[2] Female 3. Ethnicity: ……

If eligible and not in study, circle reason:
1 Refused
2 Contact made but not recruited (e.g. left message)
3 Other (specify)……..

If refusal, circle reason:
1 Time constraints/ work commitments
2 Other (specify)……
3 No reason given

NON-CONTACT - circle reason:

1 Incorrect contact details
2 Deceased
3 Other (specify)……..

King's College Hospital NHS
NHS Foundation Trust

King's College London & Institute of Psychiatry
Diabetes & Mental Health Unit
Diabetes Research Group
Weston Education Centre
10 Cutcombe Road
London
SE5 9RJ

KING'S College LONDON
University of London

Participant information sheet (version 2 R&DPCT, REC No. 08/H0808/1)

The SOUL-D study: the role of psychological and social factors on diabetes outcomes in people with newly diagnosed Type 2 **d**iabetes in **Sou**th **L**ondon.

We would like to invite you to take part in a NHS-funded research study. We understand that your General Practitioner (GP) has informed you of the study because you have Type 2 diabetes and you received your diagnosis within the last 6 months. Please take time to read the following information carefully. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Part 1 – purpose of the study

In recent times there have been significant improvements made to the way diabetes services are provided. General Practitioners (GP) throughout the country are now using the same targets, treatments and screening procedures to work with their patients to achieve the best physical health and to minimise the risk and impact of diabetes complications. As part of their review, GPs now also ask 2 questions to screen for depression, because we know that this is common in people with diabetes and can have a negative impact on health. However, what we don't yet know is whether including these screening questions leads to improvements in future health. The purpose of our study is to ask people with a recent diagnosis of Type 2 diabetes to participate by giving us detailed information about their health and their lives. We will collect all the data required of a diabetes annual review, use the depression screens and complete a more thorough assessment of social factors and psychological health. We will then look to see if this information is associated with future health. We are also interested in

measuring the effects of stress, sensitivity to insulin and the role of genes as all 3 are thought to contribute to the onset and progression of conditions such as diabetes. We will therefore ask your permission to take an extra blood sample so that we can test for these factors and to store a sample of your blood for future research. The stored sample may be used for genetic testing later and you have the option to take part in the study without making this commitment. None of the blood will be used for genetic manipulation or cloning and these analyses are aimed at understanding the role of genes in diabetes. The data produced is for research only, not for clinical purposes and will not have implications for you personally.

Do I have to take part?

It is up to you to decide. We will describe the study and go through this information sheet, which we will then give to you. We will then ask you to sign a consent form to show you have agreed to take part. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

What will happen to me if I take part?

One of our researchers will contact you or your GP to find out when your next diabetes appointment is. They will arrange to meet you at the surgery after your consultation with your GP or Practice Nurse if possible. They will ask you questions about your life, how diabetes impacts on your life and questions about your psychological health. They will also access your record for more information about your diabetes. If you agree they will arrange for a blood sample to be taken which will be tested for insulin and stress hormones. If you agree, this sample will be stored for future research and a genetic analysis performed at a later date. The meeting will last approximately 60 minutes. After the first visit we will contact you once a year, for the next 2 years initially, to arrange for a repeat of the questions and blood test. The researcher would also contact your GP for information about your diabetes and any changes that have been made to your treatment. Your diabetes treatment would continue as normal. All the information you give us will be anonymised and treated confidentially.

What are the possible disadvantages or risks of taking part?

We do not foresee any disadvantages of participating in the study. However, if you were found to be badly depressed we would let you know and with your permission, we would offer to inform your GP for further treatment.

What are the possible advantages of taking part?

We cannot promise the study will help you but the information we get from this study may help improve the treatment of people with Type 2 diabetes and give us much needed information regarding the risk factors of diabetes.

Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. We will also take measures to anonymise the data you give us. You will be given this information sheet and a signed consent form to keep, if you wish.

Future research

We have funding for this research for 5 years in total but would like to continue collecting information about your diabetes for up to 20 years, so that we can see if any of the information we record now is relevant to your long term health. We would like to request your permission to continue to collect diabetes related data from your medical notes and to contact you after the present 2 year study is over.

Further information and contact details

If you would like further information about this study please contact:-

Linda East	Prof. Khalida Ismail	Prof. Stephanie Amiel
Data Manager	Co-investigator	Principal investigator
020 7848 5667	020 7848 0778	020 7848 5639

King's College Hospital NHS
NHS Foundation Trust

King's College London & Institute of Psychiatry
Diabetes & Mental Health Unit
Diabetes Research Group
Weston Education Centre
10 Cutcombe Road
London
SE5 9RJ

KING'S College LONDON
University of London

Researcher ID:
Date:

CONSENT FORM, version 2 R&DPCT, REC No. 08/H0808/1
Title of Project: SOUL-D study: the role of psychological and social factors on diabetes outcomes in people with newly diagnosed Type 2 diabetes in South London.

Please initial box

1. I confirm that I have read and understand the information sheet dated..... (version 2) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. I agree for my medical notes to be checked by the research team during the 2 years of the study ☐
4. I agree to take part in the main study ☐

Please delete the following items if you do not wish to do them:

5. I agree to a blood test for this research ☐
6. I agree for some of my blood sample to be stored for future research ☐
7. I agree for genetic analysis of my blood ☐
8. I agree for my medical notes to be accessed by the research team for a period of up to 20 years. ☐
9. I agree to be invited for further interviews after the first 2 years ☐

_____	_____	_____
Name of Patient	Date	Signature
_____	_____	_____
Name of Person taking consent	Date	Signature

Appendix III Measures: SOUL-D Clinical Record Form and Questionnaire

SOUL-D

Baseline Clinical Record Form

SOUL-D ID No.: ☐☐☐☐

Researcher ID: ☐☐

Date of entry into study: __ __/ __ __/ __ __

0.1 Participant NHS number: ☐☐☐☐☐☐☐☐☐☐

0.2 GP national code number: ☐☐☐☐☐

0.3 GP surgery: ……

0.4 GP address:……..

0.5 Laboratory site (bloods etc), please tick:

☐[1] KCH ☐[2] GSTT ☐[3] PRU ☐[4] UHL ☐[5] QMS ☐[6] Mayday
☐[7] Other……..

0.6 GP borough

☐[1] Lambeth ☐[2] Southwark ☐[3] Lewisham ☐[4] Bromley
☐[5] Other……

Entry Visit Checklist

PIS given to participant	☐ Yes	☐ No
Original consent to study files	☐ Yes	☐ No
Copy of consent to participant	☐ Yes	☐ No
Copy of consent to GP	☐ Yes	☐ No
0.7 Baseline questionnaire completed	☐[1] Yes	☐[2] No
0.8 Baseline bloods completed	☐[1] Yes	☐[2] No
0.9 Baseline CRF completed	☐[1] Yes	☐[2] No

0.10 Researcher Notes

a. Questionnaire booklet read to subject? ☐[1] Yes ☐[2] No

b. If yes, because of: ☐[1] Vision problem ☐[2] Literacy ☐[3] Other ……

0.11 Year 1 Visit Checklist

a. Consent reviewed with participant:

☐[1]Yes ☐[2]Refused ☐[3]Non-contactable

b. Questionnaire completed	☐[1] Yes	☐[2] No
c. Year 1 bloods completed	☐[1] Yes	☐[2] No
d. Year 1 CRF completed	☐[1] Yes	☐[2] No

0.12 Year 2 Visit Checklist

a. Consent reviewed with participant:

☐[1]Yes ☐[2]Refused ☐[3]Non-contactable

b. Questionnaire completed	☐[1] Yes	☐[2] No
c. Year 2 bloods completed	☐[1] Yes	☐[2] No
d. Year 2 CRF completed	☐[1] Yes	☐[2] No

1.0 Date of data collection
___ ___ / ___ ___ / ___ ___ (dd/mm/yy)

1. Socio-demographics data

1.1 Date of birth
___ ___ / ___ ___ / ___ ___ (dd/mm/yy)

1.2 Gender
☐[1] Male
☐[2] Female

1.3 What is your legal partnership status?
Please tick the box that indicates your legal partnership status.

☐[1] Married
☐[2] Cohabitating
☐[3] Separated
☐[4] Divorced
☐[5] Widowed
☐[6] Single

1.4 Have you had children?
☐[1] Yes *If yes, please list how many*_____
☐[2] No

1.5 What is your ethnic group?
Choose ONE section from a. to e., then tick the appropriate box to indicate your ethnic group.

a. White
☐[1] British
☐[2] Irish
☐[3] Any Other White background, *please write in* ……

b. Mixed
☐[4] White and Black Caribbean
☐[5] White and Black African
☐[6] White and Asian
☐[7] Any Other Mixed background, *please write in* …….

c. Asian or Asian British
☐[8] Indian
☐[9] Pakistani
☐[10] Bangladeshi
☐[11] Any Other Asian background, *please write in* …….

d. Black or Black British

☐[12] Caribbean
☐[13] African
☐[14] Any Other Black background, *please write in ……..*

e. Chinese or other ethnic group

☐[15] Chinese
☐[16] Any Other, *please write in ……*

1.6 What is your country of birth?

☐[1] England
☐[2] Elsewhere, *please write in the present name of the country ……*

1.7 Do you consider yourself to have a faith or religious identity?

☐[1] Yes
☐[2] No

1.8 Do you attend a formal congregation or religious group?

☐[1] Yes
If yes, list group _____
☐[2] No

1.9 Employment status

Are you currently….

☐[1] In full-time employment
☐[2] In part-time employment
☐[3] On sick leave
☐[4] Unemployed
☐[5] Medically retired
☐[6] A housewife/husband
☐[7] Retired

The following questions refer to your current main job, or (if you are not working now) to your last main job. Please tick one box only per question.

1.10 Employee or self-employed
Do (did) you work as an employee or are (were) you self-employed?

☐[1] Employee
☐[2] Self-employed with employees
☐[3] Self-employed / freelance without employees (go to question 1.13)

1.11 Number of employees
For employees: Indicate below how many people work (worked) for your employer at the place where you work (worked).

For self-employed: Indicate below how many people you employ (employed). Go to question 1.13 when you have completed this question.

Please tick box.

☐[1] 1 to 24
☐[2] 25 or more

1.12 Supervisory status
Do (did) you supervise any other employees?
A supervisor or foreman is responsible for overseeing the work of other employees on a day-to-day basis.

☐[1] Yes
☐[2] No

1.13 Occupation
Please tick one box to show which **best** describes the sort of work you do.
(If you are not working now, please tick a box to show what you did in your last job).

PLEASE TICK ONE BOX ONLY.

☐[1] **Modern professional occupations**
Such as: teacher, nurse, physiotherapist, social worker, welfare officer, artist, musician, police officer (sergeant or above), software designer

☐[2] **Clerical and intermediate occupations**
Such as: secretary, personal assistant, clerical worker, office clerk, call centre agent, nursing auxiliary, nursery nurse

☐[3] **Senior mangers or administrators**
(usually responsible for planning, organising, and co-ordinating work and for finance)
Such as: finance manager, chief executive

☐[4] **Technical and craft occupations**
Such as: motor mechanic, fitter, inspector, plumber, printer, tool maker, electrician, gardener, train driver

☐[5] **Semi-routine manual and service occupations**
Such as: postal worker, machine operative, security guard, caretaker, farm worker, catering assistant, receptionist, sales assistant

☐[6] **Routine manual and service occupations**

Such as: HGV driver, van driver, cleaner, porter, packer, sewing machinist, messenger, labourer, waiter / waitress, bar staff

☐[7] **Middle or junior managers**

Such as: office manager, retail manager, bank manager, restaurant manager, warehouse manager, publican

☐[8] **Traditional professional occupations**

Such as: accountant, solicitor, medical practitioner, scientist, civil / mechanical engineer

1.14 What is your current (or last) job title?

Please write in: …….

1.15 Do you drive/hold current driving licence?

☐[1] Yes
☐[2] No

2. Diabetes history

2.1 Date of T2DM diagnosis

___ ___ / ___ ___ (mm/yy)

Diabetes Presentation:

2.2 Was participant admitted to hospital when they were diagnosed with T2DM?

☐[1] Yes
☐[2] No

2.3 Mode of Onset:

☐[1] Diabetic Symptoms
☐[2] Routine/screening blood or urine test and symptoms
☐[3] Routine/screening blood or urine test, no symptoms
☐[4] Ketoacidosis (proven) i.e. African patients
☐[5] Non-ketotic hyperosmolar (proven)
☐[6] Ketones present (not DKA)
☐[7] Diagnosed during pregnancy
☐[8] Not known

2.3 Have you attended structured diabetes education? (e.g. DESMOND)

☐[1] Yes

if yes, date (mm/yy)____/____

☐[2] No
☐[3] Waiting list

2.4 Physical examination **at diagnosis**:

Measurement	**Units**	**Value**	**Month/year (mm/yy)**
a. Height	cm		
b. Weight	kg		
c. BMI	wt/ht^2		
d. Blood pressure systolic	mmHg		
e. Blood pressure diastolic	mmHg		

2.5 Lab tests **at diagnosis**:

Test	**Units**	**Value**	**Month/year (mm/yy)**
a. Triglycerides	mmol/L		
b. LDL	mmol/L		
c. HDL	mmol/L		
d. Total cholesterol	mmol/L		
e. HbA1c	%		

2.6 Complications screening **at diagnosis**

Kidney:

2.6.1 Microalbuminuria (ACR):

a. Sample collection:

☐[1] Data not available (continue to 2.6.2)
☐[2] Early morning urine
☐[3] Random sample
☐[4] Not indicated

b. Results:

☐[1] Negative (ACR < 3)
☐[2] Positive (ACR ≥ 3)

2.6.2 Proteinuria (urine dipstick)

a. Sample Collection:

☐[1] Data not available (continue to 2.6.3)
☐[2] Early morning urine
☐[3] Random sample
☐[4] Not indicated

b. Results:

☐[1] Negative (0 – trace on urine dipstick)
☐[2] Positive (1+ - 3+ on urine dipstick)

Eyes:

Retinopathy

2.6.3 Attended DECS

☐[1] Yes
☐[2] No
☐[3] Appointment booked *(date:* ___ ___ /___ ___ / ___ ___ (dd/mm/yy))
☐[4] No appointment booked

2.6.4 DECS coding

☐[1] No retinopathy
☐[2] Treated retinopathy
(laser, photocoagulation, vitrectomy, quiescent retinopathy)
☐[3] Non-sight threatening retinopathy
(background, mild/minimal pre-proliferative, mild/moderate non-proliferative)
☐[4] Sight-threatening retinopathy
(maculopathy, moderate/severe pre-proliferative, pre-proliferative and maculopathy, non-proliferative maculopathy, at risk of and with clinically significant macula oedema)

2.6.4 Date of DECS assessment: ___ ___ / ___ ___ (mm/yy)

2.6.5 Laser treatment

☐[1] Yes
If yes, date: ___ ___ / ___ ___ (mm/yy)
☐[2] No

2.6.6 Cataracts

☐[1] Yes
☐[2] No

2.6.6 Registered partially sighted, secondary to diabetes

☐[1] Yes
If yes, date: ___ ___ / ___ ___ (mm/yy)
☐[2] No

Feet:

Foot ulcers/history of ulcer
2.6.7 R foot:

☐[1] Yes
☐[2] No
☐[3] Healed

2.6.8 L foot:

☐[1] Yes

☐[2] No
☐[3] Healed

Macrovascular disease

2.6.9 Myocardial infarction (MI) / Heart attack
☐[1] Yes
☐[2] No

2.6.10 Coronary angioplasty/CABG
☐[1] Yes
☐[2] No

2.6.11 Cerebral vascular accident (CVA) / Stroke
☐[1] Yes
☐[2] No

2.6.12 Carotid revascularisation
☐[1] Yes
If yes, date: ___ ___ / ___ ___ (mm/yy)
☐[2] No

2.6.13 Limb revascularisation
☐[1] Yes
If yes, date: ___ ___ / ___ ___ (mm/yy)
☐[2] No

2.6.14 Amputation
☐[1] Yes
If yes, date: ___ ___ / ___ ___ (mm/yy)
If yes: ☐[2] Major
☐[1] Minor
☐[2] No

2.6.15 Erectile dysfunction (see recruiter booklet for explanation)
☐[1] Yes
☐[2] No

Hypoglycaemia:

2.6.16 Severe hypoglycaemia (needing 3rd party assistance, see recruiter booklet for explanation)

☐[1] Yes
☐[2] No

2.6.17 If yes how many episodes in last 12 months? ☐☐☐

2.7 QOF psychological assessment **at diagnosis**:

2.7.1 Completion of QOF 2-item depression screening
☐[1] Yes
If yes, date: ___ ___ / ___ ___ (mm/yy)
☐[2] No

2.7.2 Results: Positive depression screen
☐[1] Yes
☐[2] No *(if no, go to section 3)*

2.7.3 If positive screen, full depression screen completed? (e.g. PHQ-9, HADS)
☐[1] Yes
If yes, date: ___ ___ / ___ ___ (mm/yy)
☐[2] No

2.7.4 If positive screen, any management for depression?
☐[1] Self-help (e.g. book/leaflet)
☐[2] Anti-depressant
☐[3] Counselling
☐[4] CBT
☐[5] Diabetes specific psychological treatment (e.g. MET/MI for diabetes)
☐[6] No treatment

3. Current depression

Depression (CIS-R)

Interviewer: please tick box

3.1 Have you had a spell of feeling sad, miserable or depressed in the past month?

☐[1] Yes

☐[2] No

3.2 During the past month, have you been able to enjoy or take an interest in things as much as you usually do?

☐[1] Yes

☐[2] No

3.3 History of depressive illness?

☐[1] Yes

☐[2] No

4. Current physical/psychological status (QOF screen=grey boxes)
Date of assessment _ _/_ _/_ _

Physical examination:

	Units	**Value**
a. Height	cm	
b. Seated height	cm	
c. Leg length	difference a-b	
d. Weight	kg	
e. BMI	wt/ht^2	
f. Waist circumference	cm	
g. Blood pressure systolic	mmHg	
h. Blood pressure diastolic	mmHg	

Neuropathy assessment:

	Units	**Value**
Vibration Perception Threshold		
4.1 **R 1st toe**	volts	
4.2 **L 1st toe**	volts	
10g monofilament sensation		
Test 5 sites: 1st, 2nd, 3rd, & 5th plantar metatarsal heads and plantar aspect of great toe. If feels < 3/5, abnormal result.		
4.1 **R foot**	no. of sites	/5
4.2 **L foot**	no. of sites	/5

Foot pulses:

4.3 **R foot** dorsalis pedis	☐[1] Present ☐[2] Absent
4.4 **R foot** posterior tibial	☐[1] Present ☐[2] Absent
4.5 **L foot** dorsalis pedis	☐[1] Present ☐[2] Absent
4.6 **L foot** posterior tibial	☐[1] Present ☐[2] Absent

Depression screening:

Low mood – use answer from 3.1	☐[1] Yes ☐[2] No
Loss of interest in activities – use answer from 3.2	☐[1] Yes ☐[2] No
4.9 Positive screen (if yes to either of the above)	☐[1] Yes ☐[2] No
4.10 PHQ-9 score from participant questionnaire	

5. Current cognitive status

<u>Telephone Interview for Cognitive Status (TICS-M)</u>

Orientation

5.1 What day of the week is it?
Day

☐[1] Correct
☐[2] Incorrect

5.2 What is today's date? (day/month/year)
Day

☐[1] Correct
☐[2] Incorrect

Month

☐[1] Correct
☐[2] Incorrect

Year

☐[1] Correct
☐[2] Incorrect

5.3 What season are we in?
Season

☐[1] Correct
☐[2] Incorrect

5.4 What is your age?

☐[1] Correct
☐[2] Incorrect

5.5 What is your telephone number (including code)?
Code + number

☐[1] Correct
☐[2] Incorrect

Registration/Free recall

5.6 I'm going to read you a list of 10 words. Please listen carefully and try to remember them. When I am done, tell me as many as you can in any order. Ready?

(Read words from list below).

Now, tell me all the words you can remember.

Yes No

☐[1] ☐[2] Cabin
☐[1] ☐[2] Pipe
☐[1] ☐[2] Elephant
☐[1] ☐[2] Chest
☐[1] ☐[2] Silk
☐[1] ☐[2] Theatre
☐[1] ☐[2] Watch
☐[1] ☐[2] Whip
☐[1] ☐[2] Pillow
☐[1] ☐[2] Giant

Attention/Calculation

5.7 Please take 7 away from 100

Answer: 93

☐[1] Correct
☐[2] Incorrect

Now continue to take 7 away from what you have left over until I ask you to stop.

Answer: 86

☐[1] Correct
☐[2] Incorrect

Answer: 79

☐[1] Correct
☐[2] Incorrect

Answer: 72

☐[1] Correct
☐[2] Incorrect

Answer: 65

☐[1] Correct
☐[2] Incorrect

5.8 Please count backwards from 20 to 1.
No mistakes?

☐[1] Yes
☐[2] No

Comprehension, semantic & recent memory
5.9 What do people usually use to cut paper?
Answer: Scissors

☐[1] Correct
☐[2] Incorrect

5.10 What is the prickly green plant found in the desert?
Answer: Cactus

☐[1] Correct
☐[2] Incorrect

5.11 Who is the reigning monarch?
Answer: Elizabeth, Queen Elizabeth, Queen Elizabeth the 2nd

☐[1] Correct
☐[2] Incorrect

5.12 Who is the Prime Minister now?
Answer: Gordon Brown (if changed write in here_____)

☐[1] Correct
☐[2] Incorrect

5.13 What is the opposite of East?
Answer: West

☐[1] Correct
☐[2] Incorrect

Language/repetition
5.14 Please say this, 'Methodist Episcopal'.
Was this pronounced exactly right?

☐[1] Yes
☐[2] No

5.15 Please repeat the list of 10 words I read earlier.

Yes No

☐[1] ☐[2] Cabin
☐[1] ☐[2] Pipe
☐[1] ☐[2] Elephant
☐[1] ☐[2] Chest
☐[1] ☐[2] Silk
☐[1] ☐[2] Theatre
☐[1] ☐[2] Watch
☐[1] ☐[2] Whip
☐[1] ☐[2] Pillow
☐[1] ☐[2] Giant

NART

Interviewer:
I want you to read slowly down this list of words starting here. *(Hand patient NART word list and indicate CHORD).* After each word please wait until I say 'next' before reading the next word. I must warn you that there are many words that you probably won't recognise; in fact most people don't know them, so just have a guess at these, O.K.? Go ahead:

Column 1

5.17 CHORD (körd)
☐[1] Correct
☐[2] Incorrect

5.18 ACHE (āk)
☐[1] Correct
☐[2] Incorrect

5.19 DEPOT (dep'ō)
☐[1] Correct
☐[2] Incorrect

5.20 AISLE (īl)
☐[1] Correct
☐[2] Incorrect

5.21 BOUQUET (bōōk'ā, bōōkā', bōkā')
☐[1] Correct
☐[2] Incorrect

5.22 PSALM (säm)
☐[1] Correct
☐[2] Incorrect

5.23 CAPON (kā'pn)
☐[1] Correct
☐[2] Incorrect

5.24 DENY (di-nī)
☐[1] Correct
☐[2] Incorrect

5.25 NAUSEA (nö'si-ə, nö'zhə)
☐[1] Correct
☐[2] Incorrect

5.26 DEBT (det)

☐[1] Correct
☐[2] Incorrect

5.27 COURTEOUS (kûrt’yəs)
☐[1] Correct
☐[2] Incorrect

5.28 RAREFY (rār’i-fī)
☐[1] Correct
☐[2] Incorrect

5.29 EQUIVOCAL (i-kwiv’ə-kl)
☐[1] Correct
☐[2] Incorrect

5.30 NAÏVE (nä-ēv)
☐[1] Correct
☐[2] Incorrect

5.31 CATACOMB (kat’ə’kōōm)
☐[1] Correct
☐[2] Incorrect

5.32 GAOLED (jāld)
☐[1] Correct
☐[2] Incorrect

5.33 THYME (tīm)
☐[1] Correct
☐[2] Incorrect

5.34 HEIR (àr)
☐[1] Correct
☐[2] Incorrect

5.35 RADIX (rā’diks)
☐[1] Correct
☐[2] Incorrect

5.36 ASSIGNATE (as’-ig-nāt)
☐[1] Correct
☐[2] Incorrect

5.37 HIATUS (hī-ā’təs)
☐[1] Correct
☐[2] Incorrect

5.38 SUBTLE (sut’l)
☐[1] Correct
☐[2] Incorrect

5.39 PROCREATE (prō’kri-àt)
☐[1] Correct
☐[2] Incorrect

5.40 GIST (jist)
☐[1] Correct
☐[2] Incorrect

5.41 GOUGE (gowj)
☐[1] Correct
☐[2] Incorrect

Column 2

5.42 SUPERFLUOUS (sōō-pûr’flŏŏ-əs, sū-pûr’flŏŏ-əs)
☐[1] Correct
☐[2] Incorrect

5.43 SIMILE (sim’i-li)
☐[1] Correct
☐[2] Incorrect

5.44 BANAL (bən-al’)
☐[1] Correct
☐[2] Incorrect

5.45 QUADRUPED (kwod’rŏŏ-ped)
☐[1] Correct
☐[2] Incorrect

5.46 CELLIST (chel’ist)
☐[1] Correct
☐[2] Incorrect

5.47 FAÇADE (fa-säd’)
☐[1] Correct
☐[2] Incorrect

5.48 ZEALOT (zel’ət)
☐[1] Correct
☐[2] Incorrect

5.49 DRACHM (dram)
☐[1] Correct
☐[2] Incorrect

5.50 AEON (ē'on)
☐[1] Correct
☐[2] Incorrect

5.51 PLACEBO (plə-sē'bō)
☐[1] Correct
☐[2] Incorrect

5.52 ABSTEMIOUS (ab-stē'mi-əs)
☐[1] Correct
☐[2] Incorrect

5.53 DÉTENTE (dā-tát)
☐[1] Correct
☐[2] Incorrect

5.54 IDYLL (id'il, id'əl)
☐[1] Correct
☐[2] Incorrect

5.55 PUERPERAL (pū-ûr'pər-əl)
☐[1] Correct
☐[2] Incorrect

5.56 AVER (ə-vûr')
☐[1] Correct
☐[2] Incorrect

5.57 GAUCHE (gō sh)
☐[1] Correct
☐[2] Incorrect

5.58 TOPIARY (tō'pi-ə-ri)
☐[1] Correct
☐[2] Incorrect

5.59 LEVIATHIAN (le-vi'ə-thən)
☐[1] Correct
☐[2] Incorrect

5.60 BEATIFY (bi-at'i-fi)
☐[1] Correct

☐[2] Incorrect

5.61 PRELATE (prel’it)
☐[1] Correct
☐[2] Incorrect

5.62 SIDEREAL (sī-dē’ri-əl)
☐[1] Correct
☐[2] Incorrect

5.63 DEMESNE (di-mān, di-mēn)
☐[1] Correct
☐[2] Incorrect

5.64 SYNCOPE (sing’kə-pē)
☐[1] Correct
☐[2] Incorrect

5.65 LABILE (lā’bil)
☐[1] Correct
☐[2] Incorrect

5.66 CAMPANILE (kam-pan-ē’lā, kam-pan-ē’lē)
☐[1] Correct
☐[2] Incorrect

6. Medication Review / Current Treatment

6.1 Herbal Remedies

☐[1] Yes
☐[2] No

Name	Total daily dose	Units
a.		
b.		
c.		
d.		
e.		
f.		

6.2 Diabetes tablets

☐[1] Yes
☐[2] No

Name	Total daily dose	Units
a. Metformin (Glucophage)		
b. Acarbose		
c. Repaglinide (Prandin)		
d. Nateglinide (Starlix)		
e. Glibenclamide (Daomil, Euglucon)		
f. Gliclazide (Diamicron)		
g. Glimepiride (Amaryl)		
h.Glipizide (Glibenese, Minodiab)		
i. Other *Name:*		

6.3 Insulin

☐[1] Yes

☐[2] No

Name	Dose (Units)	Frequency
a. Insulin Lispro (Humalog)		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:
b. Insulin Aspart (NovoRapid)		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:
c. Insulin Glulisine (Apidra)		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:
d. Insulin Glargine (Lantus)		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:
e. Isophane Insulin (NPH) (eg. Insulatard, Humulin I)		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:
f. Soluble Insulin (eg. Humulin S, Actrapid)		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:
g. Insulin Detemir (Levemir)		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:
h. Humalog Mix 25		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:
i. Humalog Mix 50		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:
j. NovoMix 30 (eg. Mixtard 30)		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:
k. Other *Name:*		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:

6.4 Cholesterol – lowering medications

☐[1] Yes

☐[2] No

Name	Total daily dose	Units
a. Atvorvastatin (Lipitor)		
b. Simvastatin (Zocor)		
c. Bezafibrate (Bezalip)		
d. Fenofibrate (Lipantil)		
e. Colestyramine (Questran)		
f. Ezetumibe		
g. Other *Name:*		

6.5 Anti-hypertensives

☐[1] Yes
☐[2] No

Name	Total daily dose	Units
a. Amlodopine		
b. Ramipril (Lopace)		
c. Doxazosin		
d. Felodipine		
e. Labetalol		
f. Atenolol		
g. Other *Name:*		

6.6 Diuretics

☐[1] Yes
☐[2] No

Name	Total daily dose	Units
a. Bendroflumethiazide		
b. Furosemide		
c. Spirinolactone		
d. Hydrochlorathiazide		
e. Other *Name:*		

6.7 NSAIDS and Opiods

☐[1] Yes
☐[2] No

Name	Total daily dose	Units
a. Aspirin		
b. Ibruprofen		
c. Codeine		
d. Hydromorphone (Dilaudid)		
e. Meperidine		
f. Oxycodone		
g. Other *Name:*		

6.8 Other medications

☐[1] Yes

☐[2] No

Name	Total daily dose	Units
a.		
b.		
c.		
d.		
e.		

7. SOUL-D Lab Tests

Date obtained: ___ ___/ ___ ___ (mm/yy)

Lab: ☐[1] KCH ☐[2] GSTT ☐[3] PRU ☐[4] UHL ☐[5] QMS ☐[6]Mayday☐[7]
Other……..

Test	Units	Value	Ref. range
Lipids			
a. Triglycerides	mmol/L		
b. LDL	mmol/L		
c. HDL	mmol/L		
d. Total cholesterol	mmol/L		
LFTs			
e. ALT (alanine aminotransferase)	IU/L		
f. AST (aspartate aminotransferase)	IU/L		
g. ALP (alkaline phosphatase)	IU/L		30-130
h. GGT (gamma-glutamyl transferase)	IU/L		1-55
Renal			
i. Creatinine	umol/L		45-120
j. eGFR	ml/min		
FBC			
k. Total white count (WBC)	10\S\9/l		4.00-11.00
l. Haemoglobin (Hb)	g/dl		11.5-15.5
m. Platelet count (PLT)	10\S\9/l		150-450
n. Neutrophils	10\S\9/l		0.20-6.30
o. Lymphocytes	10\S\9/l		1.30-4.00
TFTs			
p. Thyroid stimulating hormone (TSH)	mU/L		0.30-5.50)
q. Free thyroxine	pmol/L		9.0-25.0
r. HbA1c	%		
s. Prolactin	mU/L		< 510mU
t. C-reactive Protein	mg/l		< 5.0
u. Cortisol	nmol/L		130-580
v. Insulin levels	mU/L		4.4-26.0
u. Plasma glucose (fasting)	mmol/L		3.0-6.0
w. HOMA-IR (v x u)/22.5			
x. ACR	µg/mg		

Clinical Record Form
24 months

SOUL-D ID No.: ☐☐☐☐

Researcher ID: ☐☐

Date of 24 months follow-up: __ __/ __ __/ __ __

SOUL-D Data Collection Schedule

0.1 Year 2 Visit Checklist

a. Consent reviewed with participant:

☐[1]Yes ☐[2]Withdrawn ☐[3]Non-contactable ☐[4] Dead

b. Questionnaire completed ☐[1] Yes ☐[2] No

c. Year 2 bloods completed ☐[1] Yes ☐[2] No

d. Year 2 CRF completed ☐[1] Yes ☐[2] No

0.2 Withdrawals, non-contactables, deaths:

a. Withdrawn Date __ __/__ __/__ __

NB: please complete sections of the CRF using GP records and ensure data manager aware so that no further study letters sent out

b. Non-contactable

Date last seen at GP practice __ __/__ __/__ __

NB: please check dates of last prescription uptake as well as general records and complete sections of the CRF using GP records

c. If dead

Date __ __/__ __/__ __ Cause ……..

d. Main cause of death:

Non-specific CVD ☐[1]

MI ☐[2]

CVA ☐[3]

Infection ☐[4]

Cancer ☐[5]

Renal failure ☐[6]

Complications from liver disease ☐[7]

NB: please complete sections of the CRF using GP records

SOUL-D Data Collection Schedule

1. Socio-demographics data

1.1 What is your legal partnership status?
Please tick the box that indicates your legal partnership status.

☐[1] Married
☐[2] Cohabitating
☐[3] Separated
☐[4] Divorced
☐[5] Widowed
☐[6] Single

1.2 Employment status

Are you currently….

☐[1] In full-time employment
☐[2] In part-time employment
☐[3] On sick leave
☐[4] Unemployed
☐[5] Medically retired
☐[6] A housewife/husband
☐[7] Retired

1.3 If not working are you in full-time education?
☐[1] Yes
☐[2] No

1.4 Have you attended structured diabetes education? (e.g. DESMOND)

☐[1] Yes
if yes, date (mm/yy)____/____
☐[2] No
☐[3] Waiting list

SOUL-D Data Collection Schedule

2.0 Diabetes complications screening at 24 months

Kidney:

2.1 Microalbuminuria (ACR):

a. Sample collection:
☐[1] Data not available (continue to 2.6.2)
☐[2] Early morning urine
☐[3] Random sample
☐[4] Not indicated

b. Results:
☐[1] Negative (ACR < 3)
☐[2] Positive (ACR ≥ 3)

2.2 Proteinuria (urine dipstick)

a. Sample Collection:
☐[1] Data not available (continue to 2.6.3)
☐[2] Early morning urine
☐[3] Random sample
☐[4] Not indicated

b. Results:
☐[1] Negative (0 – trace on urine dipstick)
☐[2] Positive (1+ - 3+ on urine dipstick)

Eyes:

Retinopathy
2.3 Attended DECS
☐[1] Yes
☐[2] No
☐[3] Appointment booked *(date:* ___ ___ /___ ___ / ___ ___ (dd/mm/yy))
☐[4] No appointment booked

2.4 DECS coding
☐[1] No retinopathy
☐[2] Treated retinopathy
(laser, photocoagulation, vitrectomy, quiescent retinopathy)
☐[3] Non-sight threatening retinopathy
(background, mild/minimal pre-proliferative, mild/moderate non-proliferative)
☐[4] Sight-threatening retinopathy
(maculopathy, moderate/severe pre-proliferative, pre-proliferative and maculopathy, non-proliferative maculopathy, at risk of and with clinically significant macula oedema)

2.5 Date of last DECS assessment: ___ ___ / ___ ___ (mm/yy)

2.6 Laser treatment
☐[1] Yes
If yes, date: ___ ___ / ___ ___ (mm/yy)
☐[2] No

2.7 Cataracts
☐[1] Yes
☐[2] No

2.8 Registered partially sighted, secondary to diabetes
☐[1] Yes
If yes, date: ___ ___ / ___ ___ (mm/yy)
☐[2] No

Feet:

Foot ulcer since baseline visit
2.9 R foot:
☐[1] Yes
☐[2] No
☐[3] Healed

2.10 L foot:
☐[1] Yes
☐[2] No
☐[3] Healed

Macrovascular disease since baseline visit
2.12 Myocardial infarction (MI) / Heart attack
☐[1] Yes
☐[2] No

2.13 Coronary angioplasty/CABG
☐[1] Yes
☐[2] No

2.14 Cerebral vascular accident (CVA) / Stroke
☐[1] Yes
☐[2] No

2.15 Carotid revascularisation
☐[1] Yes
If yes, date: ___ ___ / ___ ___ (mm/yy)
☐[2] No

2.16 Limb revascularisation
☐[1] Yes
If yes, date: ___ ___ / ___ ___ (mm/yy)
☐[2] No

2.17 Amputation
☐[1] Yes
If yes, date: ___ ___ / ___ ___ (mm/yy)
If yes: ☐[2] Major
☐[1] Minor
☐[2] No

2.18 Erectile dysfunction (see recruiter booklet for explanation)
☐[1] Yes
☐[2] No

Hypoglycaemia:
2.19 Severe hypoglycaemia (needing 3rd party assistance, see recruiter booklet for explanation)

☐[1] Yes
☐[2] No

2.20 If yes how many episodes in last 12 months? ☐☐☐

3. Current depression

Depression (CIS-R)
Interviewer: please tick box
3.1 Have you had a spell of feeling sad, miserable or depressed in the past month?
☐[1] Yes
☐[2] No

3.2 During the past month, have you been able to enjoy or take an interest in things as much as you usually do?
☐[1] Yes
☐[2] No

3.3 Any management for depression since baseline?
☐[1] Self-help (e.g. book/leaflet)
☐[2] Anti-depressant
☐[3] Counselling
☐[4] CBT
☐[5] Diabetes specific psychological treatment (e.g. MET/MI for diabetes)
☐[6] Combined Treatment
☐[7] No treatment

Family history of Depression:
3.4 1st degree relatives (do not record step family only blood relations)

	Yes[1]	No[2]	Not known[3]	Number (c, d, e only)
a. Mother				
b. Father				
c. Brother (n)				
d. Sister (n)				
e. Child (n)				

SOUL-D Data Collection Schedule

4. Current physical/psychological status (QOF screen=grey boxes)
Date of assessment _ _ / _ _ / _ _

Physical examination:

	Units	Value
a. Height	cm	
b. Weight	kg	
c. BMI	kg/m^2	
d. Waist circumference	cm	
e. Blood pressure systolic	mmHg	
f. Blood pressure diastolic	mmHg	

Neuropathy assessment:

	Units	Value
Vibration Perception Threshold		
4.1 **R 1st toe**	volts	
4.2 **L 1st toe**	volts	
10g monofilament sensation		
Test 5 sites: 1st, 2nd, 3rd, & 5th plantar metatarsal heads and plantar aspect of great toe. If feels < 3/5, abnormal result.		
4.1 **R foot**	no. of sites	
4.2 **L foot**	no. of sites	

Foot pulses:

4.3 **R foot** dorsalis pedis	☐1 Present ☐2 Absent
4.4 **R foot** posterior tibial	☐1 Present ☐2 Absent
4.5 **L foot** dorsalis pedis	☐1 Present ☐2 Absent
4.6 **L foot** posterior tibial	☐1 Present ☐2 Absent

Depression screening:

Low mood – use answer from 3.1	☐1 Yes ☐2 No
Loss of interest in activities – use answer from 3.2	☐1 Yes ☐2 No
4.9 Positive screen (if yes to either of the above)	☐1 Yes ☐2 No
4.10 PHQ-9 score from participant questionnaire	

4.11 Blood glucose level		mmols/L

5. Current cognitive status

Telephone Interview for Cognitive Status (TICS-M)
Orientation
5.1 What day of the week is it?
Day

☐[1] **Correct**
☐[2] **Incorrect**

5.2 What is today's date? (day/month/year)
Day

☐[1] **Correct**
☐[2] **Incorrect**

Month

☐[1] **Correct**
☐[2] **Incorrect**

Year

☐[1] **Correct**
☐[2] **Incorrect**

5.3 What season are we in?
Season

☐[1] **Correct**
☐[2] **Incorrect**

5.4 What is your age?

☐[1] **Correct**
☐[2] **Incorrect**

5.5 What is your telephone number (including code)?
Code + number

☐[1] **Correct**
☐[2] **Incorrect**

SOUL-D Data Collection Schedule

Registration/Free recall
5.6 I'm going to read you a list of 10 words. Please listen carefully and try to remember them. When I am done, tell me as many as you can in any order. Ready?

(Read words from list below).

Now, tell me all the words you can remember.
Yes No
☐[1] ☐[2] Cabin
☐[1] ☐[2] Pipe
☐[1] ☐[2] Elephant
☐[1] ☐[2] Chest
☐[1] ☐[2] Silk
☐[1] ☐[2] Theatre
☐[1] ☐[2] Watch
☐[1] ☐[2] Whip
☐[1] ☐[2] Pillow
☐[1] ☐[2] Giant

Attention/Calculation
5.7 Please take 7 away from 100
Answer: 93

☐[1] **Correct**
☐[2] **Incorrect**

Now continue to take 7 away from what you have left over until I ask you to stop.
Answer: 86

☐[1] **Correct**
☐[2] **Incorrect**

Answer: 79

☐[1] **Correct**
☐[2] **Incorrect**

Answer: 72

☐[1] **Correct**
☐[2] **Incorrect**

Answer: 65

☐[1] **Correct**
☐[2] **Incorrect**

5.8 Please count backwards from 20 to 1.
No mistakes?

☐[1] **Yes**
☐[2] **No**

Comprehension, semantic & recent memory
5.9 What do people usually use to cut paper?
Answer: Scissors

☐[1] **Correct**
☐[2] **Incorrect**

5.10 What is the prickly green plant found in the desert?
Answer: Cactus

☐[1] **Correct**
☐[2] **Incorrect**

5.11 Who is the reigning monarch?
Answer: Elizabeth, Queen Elizabeth, Queen Elizabeth the 2nd

☐[1] **Correct**
☐[2] **Incorrect**

5.12 Who is the Prime Minister now?
Answer: David Cameron (if changed write in here_____)

☐[1] **Correct**
☐[2] **Incorrect**

5.13 What is the opposite of East?
Answer: West

☐[1] **Correct**
☐[2] **Incorrect**

Language/repetition

5.14 Please say this, ‘Methodist Episcopal’.
Was this pronounced exactly right?

☐[1] **Yes**
☐[2] **No**

5.15 Please repeat the list of 10 words I read earlier.

Yes	No	
☐[1]	☐[2]	Cabin
☐[1]	☐[2]	Pipe
☐[1]	☐[2]	Elephant
☐[1]	☐[2]	Chest
☐[1]	☐[2]	Silk
☐[1]	☐[2]	Theatre
☐[1]	☐[2]	Watch
☐[1]	☐[2]	Whip
☐[1]	☐[2]	Pillow
☐[1]	☐[2]	Giant

SOUL-D Data Collection Schedule

6. Medication Review / Current Treatment

6.1 Herbal Remedies
☐[1] Yes
☐[2] No

Name	Total daily dose	Units
a.		
b.		
c.		
d.		
e.		
f.		

6.2 Diabetes tablets
☐[1] Yes
☐[2] No

Name	Total daily dose	Units
a. Metformin (Glucophage)		
b. Acarbose		
c. Repaglinide (Prandin)		
d. Nateglinide (Starlix)		
e. Glibenclamide (Daomil, Euglucon)		
f. Gliclazide (Diamicron)		
g. Glimepiride (Amaryl)		
h. Glipizide (Glibenese, Minodiab)		
i. Other *Name:*		

6.3 Insulin
☐[1] Yes
☐[2] No

Name	Dose (Units)	Frequency
a. Insulin Lispro (Humalog)		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:
b. Insulin Aspart (NovoRapid)		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:
c. Insulin Glulisine (Apidra)		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:
d. Insulin Glargine (Lantus)		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:
e. Isophane Insulin (NPH) (eg. Insulatard, Humulin I)		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:
f. Soluble Insulin (eg. Humulin S, Actrapid)		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:
g. Insulin Detemir (Levemir)		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:
h. Humalog Mix 25		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:
i. Humalog Mix 50		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:
j. NovoMix 30 (eg. Mixtard 30)		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:
k. Other *Name:*		☐ Once daily ☐ Twice daily ☐ Three times daily ☐ Other:

6.4 Cholesterol – lowering medications
☐[1] Yes
☐[2] No

Name	Total daily dose	Units
a. Atvorvastatin (Lipitor)		
b. Simvastatin (Zocor)		
c. Bezafibrate (Bezalip)		
d. Fenofibrate (Lipantil)		
e. Colestyramine (Questran)		
f. Ezetumibe		
g. Other *Name:*		

6.5 Anti-hypertensives
☐[1] Yes
☐[2] No

Name	Total daily dose	Units
a. Amlodopine		
b. Ramipril (Lopace)		
c. Doxazosin		
d. Felodipine		
e. Labetalol		
f. Atenolol		
g. Other *Name:*		

6.6 Diuretics
☐[1] Yes
☐[2] No

Name	Total daily dose	Units
a. Bendroflumethiazide		
b. Furosemide		
c. Spirinolactone		
d. Hydrochlorathiazide		
e. Other *Name:*		

6.7 NSAIDS and Opiods
☐[1] Yes
☐[2] No

Name	Total daily dose	Units
a. Aspirin		
b. Ibruprofen		
c. Codeine		
d. Hydromorphone (Dilaudid)		
e. Meperidine		
f. Oxycodone		
g. Other *Name:*		

6.8 Other medications
☐[1] Yes
☐[2] No

Name	Total daily dose	Units
a.		
b.		
c.		
d.		
e.		
f.		
g.		
h.		
i.		
j.		
k.		

SOUL-D Data Collection Schedule

7. SOUL-D Lab Tests

Date obtained: ___ ___/ ___ ___ (mm/yy)

Lab: ☐[1] KCH ☐[2] GSTT ☐[3] PRU ☐[4] UHL ☐[5] QMS ☐[6]Mayday ☐[7] Other……..

Test	Units	Value	Ref. range
Lipids			
a. Triglycerides	mmol/L		0.5-2.0
b. LDL	mmol/L		1.0-3.0
c. HDL	mmol/L		>1.0
d. Total cholesterol	mmol/L		1.0-5.0
LFTs			
e. ALT (alanine aminotransferase)	IU/L		5-55
f. AST (aspartate aminotransferase)	IU/L		10-50
g. ALP (alkaline phosphatase)	IU/L		30-130
h. GGT (gamma-glutamyl transferase)	IU/L		1-55
Renal			
i. Creatinine	umol/L		45-120
j. eGFR	ml/min		
FBC			
k. Total white count (WBC)	10\S\9/l		4.00-11.00
l. Haemoglobin (Hb)	g/dl		11.5-15.5
m. Platelet count (PLT)	10\S\9/l		150-450
n. Neutrophils	10\S\9/l		0.20-6.30
o. Lymphocytes	10\S\9/l		1.30-4.00
TFTs			
p. Thyroid stimulating hormone (TSH)	mU/L		0.30-5.50
q. Free thyroxine	pmol/L		9.0-25.0
r. HbA1c	%		<7.5%
s. Prolactin	mU/L		< 410
t. C-reactive Protein	mg/l		< 5.0
u. Cortisol	nmol/L		130-580
v. Insulin levels	mU/L		4.4-26.0
w. Plasma glucose (fasting)	mmol/L		3.0-6.0
x. HOMA-IR (v x u)/22.5			
y. ACR	µg/mg		<3.0

Appendix IV Data from external sources

Points of Interest (POI) Codes

Fast food outlets

01020018 Fast food and takeaway outlets

01020019 Fast food delivery services

01020020 Fish and chip shops

01020661 Bakeries

Green spaces

03180252 Commons

03180253 Country and national parks

03180254 Picnic areas

03180255 Playgrounds

Sports facilities

04240289 Athletics facilities

04240291 Climbing facilities

04240292 Golf ranges, courses, clubs and professionals

04240293 Gymnasiums, sports halls and leisure centres

04240302 Sports grounds, stadia and pitches

04240303 Squash courts

04240304 Swimming pools

04240305 Tennis facilities

04240306 Velodromes

Appendix IV Statistical Analyses

Results from the tests of interaction

Table 26 Tests of interaction between social support variables and stratified variables

Interaction	F ratio	p value
Gender*Perceived social support	1.21	0.27
Gender*Marital status	1.39	0.25
Gender *Social network	1.09	0.37
Gender*Community ties	0.66	0.42
Depression*Perceived social support	0.05	0.83
Depression*Marital status	0.97	0.41
Depression *Social network	1.67	0.08
Depression*Community ties	0.32	0.57
Ethnicity*Perceived social support	0.17	0.85
Ethnicity*Marital status	1.12	0.35
Ethnicity *Social network	0.76	0.77
Ethnicity*Community ties	0.30	0.74